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OCULAR EFFECTS OF ALTITUDE FLYING AND OF DEEP SEA DIVING

CAPTAIN LEON D CARSON (MC), U.S.N

The subject assigned refers primarily to changes brought about by alterations in atmospheric pressure and in partial pressure of oxygen, to rapid and severe changes in temperature and to protection of the eyes against glare, air blast, dust and flying debris. Changes in atmospheric pressure in flying are within the range between the pressure at sea level (1 atmosphere—about 15 pounds per square inch [1,050 Gm per square centimeter], or 760 mm of mercury) and a pressure of about $\frac{1}{6}$ atmosphere ($2\frac{1}{2}$ pounds per square inch [170 Gm per square centimeter], or 127 mm of mercury) at the maximum altitudes now attainable by military aircraft. Pressures encountered in deep sea diving can also be expressed in terms of pressure at sea level. These pressures range from 1 to 6, 7 or 8 atmospheres.

The physiologic effects of variations in pressure are brought about in several ways:

- 1 By increase or decrease in the partial pressure of the oxygen

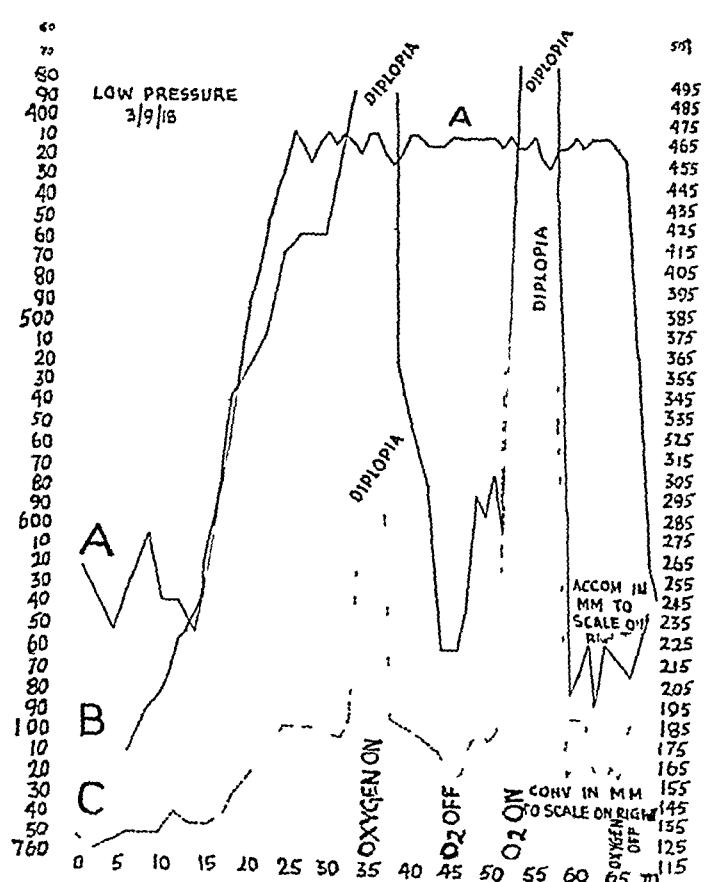
- 2 By rapid decompression of the envelope of air around the earth, resulting in escape of inert gases from solution in bodily fluids and tissues in the form of bubbles, or air emboli, which tend to obstruct capillaries and small blood vessels and to produce disturbances of function through localized ischemia or through direct pressure on the brain and nerve tissues

- 3 Through the toxic effects of oxygen. These effects have been reported occasionally at greatly increased pressures, such as those experienced by divers, and also when oxygen was added to inspired air.

As can be seen from the foregoing remarks, ocular effects may occur either as part of a general anoxic syndrome or as accidents resulting from localized obstruction or from phenomena due to direct pressure which affect the nutrition of the retina or the innervation of the intrinsic or extrinsic ocular muscles.

Inasmuch as military flying at altitudes above 10,000 feet (3,300 meters) requires the use of oxygen, severe degrees of anoxia are not often

encountered. However, failure of the supply of oxygen or leakage of masks at great altitudes may cause rapidly developing and severe anoxia, with a resultant general picture of failure of special senses, impairment of judgment, loss of consciousness, motor convulsions and anoxic death if the situation is not speedily corrected.



The effect on accommodation and convergence of simulated altitude in the low pressure chamber. *A*, curve of accommodation plotted against figures in millimeters on the right. *B*, curve of barometric pressure plotted against barometric pressure in millimeters on the left. *C*, curve of convergence plotted against a millimeter scale on the right. Note that accommodation and convergence fail when the barometric pressure drops to 400 mm of mercury. Accommodation and convergence are immediately restored to normal by the administration of oxygen, even though the barometric pressure remains at 400 mm.

Certain effects of even slight or low grade anoxia are reflected in vision to some degree. Prolonged flight at an altitude of 8,000 to 10,000 feet (2,600 to 3,300 meters) causes slight but measurable impairment of retinal response, such as can be demonstrated by diminished perception of low contrast images, increased threshold of

light sensitivity as demonstrated by the adaptometer test and impaired flicker-fusion response. Slight anoxia has such a definite effect on the sensitivity of the retinal rods that military fliers are advised to cut in their supply of oxygen from the ground on up in combat flying at night. In runs in the low pressure chamber to simulated high altitudes without added oxygen, reduction in visual acuity has been observed in 28 to 65 per cent of persons, color vision has also been impaired. Diminution of sensitivity to red is less than to green or to blue. Under some conditions of anoxia, green and blue signals may appear gray and completely colorless. With regard to the effect of high altitudes on the visual field, reports are somewhat conflicting. Narrowing of the fields, especially of the upper and nasal portions, has been described but this effect has been attributed by some workers to failure of attention.

Even mild anoxia has been shown to cause a considerable increase in the total area of the normal blindspot, especially under conditions of greatly reduced illumination of the object of the visual test or when low contrast test objects are used. A fasting level of blood sugar exerts a similar effect or may be additive to mild anoxia. In ascents in the low pressure chamber to the equivalent of 19,000 feet (6,000 meters), the area of the blindspot has been found to increase as much as two and one-half times. Reduction to the normal area occurs on the subject's breathing oxygen or on his descent to sea level pressure.

Decrease in intraocular tension at simulated altitudes of 12,000 to 19,000 feet (4,000 to 6,000 meters) in human subjects has been reported although if low pressure is prolonged the tension tends to return to normal. Pinson¹ in 1940 found no significant changes in intraocular tension in a rabbit decompressed to the equivalent of 40,000 feet (12,000 meters).

In deep sea diving higher pressures are involved, so that anoxia does not play a part. However, disturbances of vision or of muscle balance can be occasioned by a rather infrequent phenomenon known as oxygen intoxication.

Similar systemic effects believed to be caused by nitrogen narcosis have been described in the literature on this subject.

Diplopia, scotomas and amaurosis occur occasionally as a result of sudden reduction of pressure and release of inert gases from saturation. Air emboli probably lodge in the bulbar nuclei within the optic tract or in the visual cortex, although attempts to demonstrate such phenomena are extremely difficult and have

all failed. Investigators have occasionally reported seeing emboli passing through the retinal vessels and through the meningeal vessels which are visible when the calvaria of an experimental animal is removed. Oculomotor disturbances caused by aeroembolism are infrequent, paresthesias, pruritus and other conditions may persist for six to eight hours after exposure to changing pressures but often are of brief duration. The mechanism is not clearly understood.

An indication of the range of ocular disturbances which may be encountered in high altitude flying is given in the following list of complaints referable to the eyes in persons given runs in the low pressure chamber for the purpose of indoctrination. The symptoms are reported as persisting from one to sixty hours: (1) partial blindness, (2) right homonymous hemianopsia, (3) bilateral binasal blurring, (4) nystagmus, (5) spots before the eyes, (6) scintillating scotomas, (7) diplopia, (8) yellow vision and (9) ocular pain.

In addition to phenomena ascribable to lowered partial pressure of oxygen at higher altitudes and to sudden and radical changes in atmospheric pressure, one other problem of some importance has attracted the interest of ophthalmologists. This is the dazzling effect of excessive solar light at upper atmospheric levels. Occasional complaints of excessive brightness at great altitudes are heard. Careful inspection usually fails to demonstrate any unusual local reaction, such as injection of the pupil or ciliary spasm.

For a number of years the medical profession has shown considerable interest in the possible injurious effects of solar rays lying beyond the range of the visible spectrum. The most important in the present connection are the heat waves, the infra-red rays, the visual rays and the ultraviolet rays. Of the waves emitted by the sun, part are completely destroyed in the atmosphere, part are absorbed and part reach the earth. The intensity of all these waves increases with altitude, as the density of the absorbing atmospheric layer decreases. In higher mountains and in flight, therefore, the exposure to ultraviolet, to visible and to infra-red rays is greater than at lower altitudes. Severe sunburn frequently occurs because of exposure to ultraviolet rays, but it has been generally observed that the tolerance of the unprotected eye is apparently considerably greater than that of the skin and of the mucocutaneous junctions. The once hypothesized probability of danger to the eyes from excessive exposure either to infra-red or to ultraviolet rays at high altitude is not now regarded with as great concern as formerly.

¹ Pinson, E. A. Intra-Ocular Pressure at High Altitudes, *T Aviation Med* 11: 108-111, 1940.

At altitudes requiring the administration of oxygen a mask is worn which protects most of the face. Also, because of the painful glare it is necessary to employ goggle lenses or spectacle lenses which have been tinted so as considerably to reduce the total transmission of light. These glare-reducing protective lenses must, of course, comply with the same standards of optical measurement as any other good spectacle lenses. In aerial combat the goggles must also serve to protect the eyes against flash and against flying bits of metal.

Many problems still exist relative to goggles for flying. The ideal goggles for flying should possess the following characteristics:

1 They should afford adequate protection against glare, against air blast and against flying debris, dust and flash burn.

2 They should provide a totally unrestricted visual field for each eye. Goggles at present issued seriously restrict the nasal portion of each visual field.

3 They should be so designed as to integrate well with the upper portion of an oxygen mask and still fit snugly about the nose and the infra-orbital area when the oxygen mask is not being worn.

4 They should afford maximum comfort.

5 They should be so ventilated as to be free from fogging or frosting.

6 They should contain no metal or shatterable glass to cause ocular or orbital injury on crash landings.

7 Finally, they should be free from optical error.

Recently a type of goggles has been developed by the Aviation Section, Research Division of the Bureau of Medicine and Surgery, United States Navy Department, which approaches these requirements, and these are now being issued as alternate or optional equipment. With these goggles are supplied quickly interchangeable lenses of two colors and densities along with two extra clear lenses.

The pilot's and the gunner's vision are of the greatest importance in military flying. Workers in the field of aviation medicine must be concerned not only about such matters as the design for goggles but also about the design of the airplane itself in their efforts to provide the best possible vision for the flying personnel. The quality of clear plastic windshields, radomes and gunners' plastic enclosures are matters of vital concern. Much is being done to improve these mediums.

ABSTRACT OF DISCUSSION

DR CONRAD BERENS, New York. Although there is little I can add to Captain Carson's splendid contribution, it is a privilege to discuss a paper on the subject of changes in atmospheric pressure as they affect ocular functions by a man who has had so much practical experience in this field. Because reference has been made to the fact that I worked in this field during the last war, it occurred to me that some historical points might be of interest, since much of the new information is secret.

When the United States entered the First World War, the only allusions to altitude in its relation to ocular functions referred to experiments in the low pressure chamber by the great French pioneer, Paul Bert, and others. Balloonists at times mentioned the difficulty of seeing the column of mercury in the barometer at high altitudes. Sometimes mountain climbers noticed a failure of vision or, more often, of accommodation. There was still some question of the exact cause for the physical and ocular disturbances produced by altitude, in spite of the excellent work of Henderson, Schneider, Haldane and Dwyer on Mount McKinley.

I was fortunate in having Drs Schneider, Henderson and Dwyer to work with me in my original investigations. Our group, which included three members of this section, namely, Drs Dunnington, Webster and Skeel, soon found that at the altitudes at which we worked, up to about 28,000 feet (9,000 meters) for most of the runs in the low pressure chamber or in the rebreathing apparatus, the administration of oxygen almost immediately restored ocular functions to normal, and that this occurred when the barometric pressure was held constant. In a paper published in 1918 we concluded that the lowered visual acuity, the lowered retinal sensitivity to white and to colored light, the contraction of the visual and binocular fields and the weakening of accommodation, convergence, divergence and supravergence were caused mainly by lack of oxygen and were not due to the many other suggested conditions, such as lowered blood pressure, decreased atmospheric pressure, carbon monoxide, nervous strain and vibration of the motor. In our experience, the administration of oxygen prevented the occurrence of the untoward symptoms, and when these symptoms occurred through its want oxygen quickly restored the functions to normal.

One of our records, made in 1918, of the effect of the administration of oxygen on convergence and accommodation while the atmospheric pressure was held constant at low level is shown in figure 1.

I am particularly interested in Captain Carson's discussion of altitude in flying and the relative infrequency of acute anoxic ocular symptoms. I understand that most of the bombing at night by British planes is done at about 20,000 feet (7,000 meters) and that a great deal of the bombing by American planes in daylight is done at 27,000 feet (9,000 meters) and lower. Therefore, only under the circumstances that Captain Carson cited will acute symptoms of aeroembolism arise. I have had no experience with the toxic effects of oxygen which he discussed.

His account of the effects of prolonged flights below 10,000 feet (3,300 meters) is most interesting, as we had already concluded from our original investigations that the eyes would be affected only by prolonged exposure to this altitude. In studying this type of flight it was hard to eliminate other factors which are now known to produce flying fatigue.

In the low pressure chamber we had no experience with aeroembolism, and the planes used in the first World War did not attain 35,000 feet (12,000 meters). Visual disturbances from aeroembolism are more com-

mon in the present conflict, but so far most of the changes reported have been transient I have heard of 1 case, however, in which visual disturbances, presumably due to aeroembolism affecting the visual cortex, apparently persisted for several days

The dazzling effect of excessive solar light has been recognized for many years We studied the various types of goggles and glass which were most effective in preventing difficulties from this source Certainly for flying over snow and water and into the sun, lenses which effectively reduce the incident light are necessary, and it is also desirable to have lenses which disturb color values as little as possible The problem today is different from that in the last war, when airplanes had open cockpits

One new angle is the question of contact lenses Commander Nichols of the Royal Canadian Air Force told me the other day that contact glasses greatly reduce efficiency in flying at night and cause troublesome dazzling in landing and in flying into the sun On the other hand, I know of one successful navy combat pilot who seems to have had no difficulty and who has made a splendid combat record

I wish Captain Carson would discuss the effects of acceleration and deceleration and of "blacking out" and "redding out," because the increasing speed of planes, especially with the new propulsion types of motors, will bring this problem more and more to the fore

CAPTAIN LEON D CARSON The review by Dr Berens of the facts of historical interest to flight surgeons is a little startling each time I hear it The work of the men who did research in this field in the past is so closely parallel to the problems which are now of current interest as to indicate what a careful study and appraisal was made of the problems as they existed at that time, problems which still exist Of course, back in 1916, 1917 and 1918 "blackout" was not a common problem in flying, since the planes were able to withstand less stress than the pilots who flew them

There are two types of acceleration that produce stress in military aircraft These are linear acceleration and acceleration in the vertical axis of the pilot (centrifugal acceleration) Linear acceleration may not be of a high order in starting and stopping except in cases of catapult shots and crash landings A great deal has been done to negate the effects of linear acceleration both in crash landings and in dogfights The development of the jet propulsion or rocket propulsion aircraft we have been reading about in the papers is going to add to our problems in this field of acceleration Acceleration is a function of the square of the velocity divided by the radius of the curve through which an airplane flies If a pilot flies an airplane around a

certain arc at a given speed, he may, by means of accelerometers, determine the multiple of g, or gravitational force, that is stressing every structure of that moving plane, as well as every structure of himself If he doubles the speed of the airplane, that is, halves the time of its flying around a given circle, he is doubling the acceleration twice (that is, 2 squared, or 4 times the amount of g) It has been determined that the human body can stand relatively high gravitational or accelerative loads provided these stresses are not applied for more than about three seconds at a time The upper limit of tolerance for gravitational stress seems to be about 4 or 4½ g's if stress is maintained during a standard interval of five seconds As this value of g is exceeded, more and more pilots are blacked out There is a rather wide range of tolerance in the human being in his response to accelerative stress Henderson, in a very good article, which was republished in *Science* two years ago and which was a review of his article on the venopressor mechanism, gave a pretty fair clue as to what is going on in the case of pilot's blackout There is no doubt that the pilot has pooling of the blood below the level of the heart and that this pooling of blood takes place in the dependent portions of the body, the extremities, the abdomen, the arms and the legs If a means can be found to protect those dependent portions of the body against engorgement due to the effects of the strong accelerative forces on the column of blood the human tolerance for that type of stress can, theoretically, be considerably increased Without going into the question of how this is done, which of course is not a matter for free discussion at the moment, I may say that there have now been used in actual flight in this country, in Australia and in Great Britain three different types of supportive devices which have been adapted to use in airplanes and which have been found to raise the average tolerance of human beings by a matter of from 2½ to 2¾ g When it is calculated in terms of actual weight that if a man weighs 150 pounds (68 Kg) and a force of 6 g is applied he bears down on his feet with 6 times 150 pounds, or 900 pounds (408 Kg), it is seen that 2½ × 150 pounds is a considerable increment of weight Experiments in this connection are still going on The Canadians have developed a huge human centrifuge and a complete biophysical laboratory, and also a fine library to go with it, and the Mayo Aeronautical Laboratory has done similarly A new human centrifuge has been installed at Wright Field, and some interesting tests are being made at Pensacola, Fla A great deal of time could be consumed in telling what tests are made in these centrifuge runs, but I am afraid lack of time will prevent a more general discussion

HERPES SIMPLEX KERATITIS IN MALARIA

CLINICAL AND EXPERIMENTAL STUDY

CAPTAIN WEBB P CHAMBERLAIN JR

AND

CAPTAIN LEWIS H BRONSON JR

MEDICAL CORPS, ARMY OF THE UNITED STATES

During recent months increasing numbers of otherwise healthy troops have contracted malaria in tropical combat areas. In these patients numerous instances of keratitis due to herpes simplex virus have been encountered. These infections have frequently resulted in serious scarring of the cornea, and the ulcers have been prone to recur with successive attacks of malaria. For these reasons it has seemed worth while to consider the relation between malarial fever and herpetic keratitis.

The most common corneal lesion of herpes simplex is an epithelial infection which is usually seen as an irregular linear ulceration with characteristic dendritic contour. Multiple discrete superficial punctate lesions may be found alone or simultaneously with a dendritic ulcer. Deep keratitis may develop from a preexisting superficial lesion or may appear as a disciform keratitis involving primarily the corneal parenchyma. A disturbing feature is the recurrence of small rounded metaherpetic ulcers. Corneal hypoesthesia is characteristic of all these manifestations. Instances of every variety of herpes simplex keratitis have been encountered in patients with recurrent malarial attacks, but this paper is chiefly concerned with superficial dendritic keratitis.

Hornei¹ in 1871 first described the dendritic ulcer as a morphologic entity and on clinical grounds suggested a possible relationship with lesions due to herpes elsewhere on the body.

In the years that followed, a number of clinicians were impressed with the frequency of this type of ulceration in malarial fever (Kipp² 1880 and 1889, Wilder³ 1893, Ellett⁴ 1899, Charles⁵

1 Horner, F Ueber Herpes cornealis, *Klin Monatsbl f Augenh* **9** 321, 1871

2 Kipp, C J On Keratitis from Malarial Fever, *Tr Am Ophth Soc* **3** 91, 1880, Further Observations on Malarial Keratitis, *ibid* **5** 331, 1889

3 Wilder, W H Dendritic Keratitis, *J A M A* **21** 604 (Oct 21) 1893

4 Ellett, E C A Series of Cases of Malarial Keratitis with a Report of Blood Examinations, *Ophth Rec* **8** 115, 1899

5 Charles, T W Dendritic Keratitis *Am J Ophth* **21**.97, 1904

1904). In the first world war large numbers of British troops were infected with malaria, and a number of cases of dendritic keratitis were reported (Kiep,⁶ Maxwell,⁷ Bywater⁸)

Because of the frequent association in onset of corneal ulcers and malarial attacks, some reports ascribed the ulcers strictly to malaria (Kipp² 1880-1889, Ellett⁴ 1899, Charles⁵ 1904, Kiep⁶ 1922, Bywater⁸ 1922). However, an increasing number of publications supported Horner's original contention that they were probably a manifestation of herpes simplex (Hagnauer⁹ 1891, Wilder³ 1893, Maxwell⁷ 1918). In discussing the question of keratitis in malaria, R H Elliot¹⁰ in his treatise "Tropical Ophthalmology" maintained a judicious attitude of skepticism in making the observations that while (1) there is an obvious association between malaria and this form of corneal ulceration, (2) the keratitis cannot be regarded as purely a manifestation of plasmodial disease.

Gruter¹¹ in 1920 first reported the existence of a specific virus in the fluid of corneal herpes simplex vesicles and showed that the disease can be transferred to the cornea of a rabbit. He likewise confirmed the common theories of the causation of the different lesions produced by this virus in the eye and about the face or the genitalia.

Extensive research has been devoted to the herpes simplex virus and also to the relation of this organism to the eye. The outstanding study

6 Kiep, W H Ocular Complications Occurring in Malaria, *Tr Ophth Soc U Kingdom* **42** 394, 1922

7 Maxwell, E M Observations on Eye Conditions Met with in Malta, 1916-17 (Occurring Among British Troops in the Balkans and Malta Garrison), *Brit J Ophth* **2** 406, 1918

8 Bywater, H H Notes on Malarial Conditions of the Eyes, *Tr Ophth Soc U Kingdom* **42** 359, 1922

9 Hagnauer, E Ueber die Misdeutungen des Herpes corneae febrilis, Zurich, Hofer & Burger, 1891, cited by Wilder³

10 Elliot, R H Tropical Ophthalmology, London, Oxford University Press, 1920, p 453

11 Gruter, W Experimentelle und klinische Untersuchungen über den sogenannten Herpes corneae, *Klin Monatsbl f Augenh* **65**.398 1920

on ocular herpes has been that of Gunderson,¹² in Boston. The present status of knowledge in this field has been recently summarized by Thygeson¹³ in his monograph "Viruses and Virus Diseases of the Eye".

Since the definitive establishment of the virus causation of dendritic keratitis there have been occasional references to an association with malaria. Finnoff¹⁴ reported 2 instances of dendritic keratitis occurring in therapeutic malaria and suggested the danger of inducing herpetic keratitis when employing malarial fever therapy for syphilis of the central nervous system. Post¹⁵ and Lloyd¹⁶ have observed that there is an apparent correlation between malaria and dendritic ulceration. Gunderson¹² recorded 1 case of malaria, and he found that the majority of the dendritic ulcers in his extensive series were associated with infections of the upper respiratory tract. Duke-Elder¹⁷ has listed influenza and pneumonia as febrile conditions frequently associated with herpetic keratitis. Berliner¹⁸ reported an instance of dendritic ulcer following artificial pyrexia induced by diathermy, while Finnoff¹⁴ and Lloyd¹⁶ mentioned foreign protein shock therapy as a precipitating factor. That fever alone does not often precipitate dendritic keratitis is evident from the fact that Solomon,¹⁹ working under Stecher at Cleveland City Hospital, did not encounter a single instance of this corneal complication in 10,000 treatments in the fever cabinet.

INCIDENCE OF HERPES KERATITIS IN MALARIA

Because of the apparent frequency with which the onset of herpes simplex keratitis has been chronologically associated with acute recurrences of malaria, it was decided to investigate the inci-

12 Gunderson, T. Herpes Corneae, with Special Reference to Its Treatment with Strong Solution of Iodine, *Arch Ophth* **15** 225 (Feb) 1936.

13 Thygeson, P. Viruses and Virus Diseases of the Eye II Viruses of Ocular Importance, *Arch Ophth* **29** 488 (March) 1943.

14 Finnoff, W C. Dendritic Keratitis Following Therapeutic Inoculation of Malaria, *Am J Ophth* **12** 978, 1929.

15 Post, M H. Dendritic Keratitis, *Am J Ophth* **12** 884, 1929.

16 Lloyd, R I. Herpes and Allied Conditions, *Am J Ophth* **14** 601, 1931.

17 Duke-Elder, W S. Textbook of Ophthalmology, London, Henry Kimpton, 1939, vol 2, 1894.

18 Berliner, M L. Herpes Cornea Occurring After Artificial Hyperpyrexia Induced by Diathermy, *Arch Ophth* **10** 365 (Sept) 1933.

19 Stecher, R M, and Solomon, W M. Complications and Hazards of Fever Therapy. Analysis of 10,000 Consecutive Fever Treatments with Kettering Hypertherm Ann Int Med **10** 1014 1937, personal communication to the authors.

dence of this type of corneal infection among malarial and among nonmalarial patients.

The new patients examined in the clinic with which we have been associated during an eighteen month period fall into two comparable groups. The first had been in a malarial district under combat conditions for four months and had a malarial incidence of about 80 per cent, but the patients were otherwise in good physical condition. The second was composed of troops free from malaria. The two divisions lived under similar camp conditions in an area where minor infections of the respiratory tract are common but primary infection with malaria is unknown.

Table 1 indicates the incidence of various types of keratitis in these two groups.

TABLE 1.—Incidence of Various Types of Keratitis Among New Eye Clinic Patients Derived (1) From Troops Exposed to Malaria and (2) From Troops Not Exposed to Malaria

	I Troops Exposed to Malaria	II Troops Not Exposed to Malaria
Total number of new patients	2,448	2,200
Superficial herpes simplex keratitis	13	2
Catarrhal ulcers	14	6
Interstitial keratitis	1	1
Meningococcal ulcer	0	1
Herpes zoster keratitis	1	1

Plasmodium vivax (the causative agent of benign tertian malarial fever) was demonstrated in blood smears from all 13 patients who had keratitis associated with herpes simplex and who had been exposed to malaria. In each patient the onset of corneal ulceration followed shortly an acute malarial recurrence. None of these patients had concomitant infections of the respiratory tract. In this limited series the incidence of dendritic keratitis in the malarial group was 1 in each 188 new patients examined in the ophthalmologic clinic, whereas among patients not exposed to malaria the incidence was 1 in each 1,100 new patients. Hence corneal infection associated with herpes simplex would seem to be about six times as frequent among troops infected with malaria. However, it is significant that only a fraction of 1 per cent of the patients admitted to the hospital with malaria ever contracted herpetic keratitis. In this study the incidence of keratitis associated with herpes simplex among new patients with acute recurrent malaria admitted to the general medical service of this hospital was less than 0.2 per cent, or about 1 in 700 patients. Although keratitis associated with herpes simplex is much more frequently encountered in a population heavily infected with malaria, the percentage of patients

with acute malaria that contract this type of keratitis remains small

TREATMENT

The management of keratitis associated with herpes simplex in malaria must be founded on energetic treatment of the malarial fever. Recurrent attacks of malaria occur even under optimum conditions and are often accompanied by reactivation or extension of the dendritic ulcer. There is no specific treatment for herpes simplex of the cornea. The generally accepted routine attempts to destroy the infected epithelium either by cautery or by curettage. Common usage favors the employment of an alcoholic solution containing 7 per cent iodine and 5 per cent potassium iodide and this has been recommended by Gundersen.¹² Local application of ether²⁰ has been suggested, and vitamin B,²¹ has been advocated as beneficial in herpetic keratitis. Frank²² has used herpes simplex vaccine, and Davis²³ spoke favorably of employment of smallpox vaccine. Schwartz²⁴ has recently emphasized the importance of removal of foci of infection in the treatment of herpes simplex corneae. No single procedure has met with uniform success.

Administration of sulfonamide compounds by mouth was favorably reported on by Kleefeld²⁵ but as Thygeson¹³ has pointed out, there is no indication from animal experimentation that the virus of herpes simplex is susceptible to chemotherapy. However, it would seem possible that secondary infection might play a part in certain instances. Furthermore, Gundersen¹² found that the virus cannot be recovered from the recurring erosions of the metaherpetic type.

In view of the good results often obtained through therapy of nonherpetic ulcerative keratitis with sulfonamide compounds, it seemed worth while to attempt an evaluation of the local use of sulfanilamide or sulfadiazine in the treat-

ment of dendritic keratitis. The powdered drug was applied twice daily to the corneal lesions. In some instances the use of a sulfonamide compound was combined with other forms of therapy. Atropine and local heat were employed in all instances, and foci of infection were eliminated when this procedure was indicated. There is considerable individual variation in the severity of dendritic ulcers and in their response to general therapy. For this reason the results of any specific treatment must be interpreted with caution.

REPORT OF CASES

CASE 1—An 18 year old white youth was admitted to the hospital on June 14, 1943 with his third acute attack of malaria. A few hours after admission he complained of irritation, tearing and photophobia in the left eye. There was no history of a similar episode or of injury. His visual acuity was 20/20 in the right eye and 20/40 in the left. A superficial ulceration of dendritic pattern involved the temporal third of the cornea. A blood smear yielded *Plasmodium vivax*. A test of the skin with herpes simplex antigen gave strongly positive results. The patient's blood serum showed antibodies capable of protecting the chorioallantoic membrane against approximately 100,000 infectious units of known herpes simplex virus.

Sulfadiazine powder was applied to the lesion twice daily for six days, with complete healing of the ulcer. When the patient was discharged to full duty, vision in the affected eye had improved to 20/30. There had been no recurrence of keratitis after two months.

CASE 2—A 27 year old white man was admitted to the hospital on May 26, 1943 with his first attack of malaria, approximately six months after leaving a malarious area. One day after admission he noticed irritation, tearing and photophobia in his left eye. There was no history of similar complaint or of injury. His visual acuity was 20/20 in the right eye and 20/20 in the left. Three discrete, irregular, star-shaped areas of superficial ulcerations were present in the pupillary area of the left eye. A blood smear yielded *Plasmodium vivax*. The patient was treated for two days with instillation of a 0.25 per cent solution of zinc sulfate and with mercury bichloride ointment 1:5,000, with no improvement. Sulfadiazine powder was then applied to the ulcer twice daily for thirteen days, with complete healing of the cornea. When the patient was discharged to full duty, vision was 20/20 in each eye. There had been no recurrence of keratitis in two months.

CASE 3—A 33 year old white man was admitted to the hospital May 25, 1943 with his third attack of acute malaria. Within twenty-four hours of his admission he noticed increasing irritation, redness and tearing in his left eye. There was no history of a similar episode or of injury. Visual acuity was 20/20 in the right eye and 20/70 in the left. Examination showed a small dendritic ulceration in the center of the pupillary area of the left eye. The blood smear yielded *Plasmodium vivax*. A cutaneous test with herpes simplex antigen gave strongly positive results. The patient's blood serum showed antibodies capable of protecting the chorioallantoic egg membrane against approximately 100,000 infectious units of known herpes simplex virus.

For twenty-four hours a 0.25 per cent solution of zinc sulfate was instilled and mercury bichloride ointment 1:3,000 employed, without alteration in the lesion.

20 Kronenberg, B. Treatment of Herpetic Keratitis with Ether. *Arch Ophth* **26**: 247 (Aug) 1941.

21 Nitzulescu, J., and Triandof, E. Treatment of Herpetic Keratitis with Vitamin B. *Brit J Ophth* **21**: 654, 1937.

22 Frank, S. B. Formalized Herpes Virus Therapy and the Neutralizing Substance in Herpes Simplex. *J Invest Dermat* **1**: 267, 1938.

23 Davis, P. L. Recurrent Herpes of the Cornea and Recurrent Herpetic Fever. Results of Treatment with Smallpox Vaccine. *J A M A* **114**: 2098 (May 25) 1940.

24 Schwartz, F. O. Treatment of Herpetic and Dendritic Ulcers. *Am J Ophth* **26**: 394, 1943.

25 Kleefeld, G. Traitement des affections herpétiques cornéennes et de l'ulcère dendritique par des dérivés sulfonamides. *Bull Soc belge d'opht* **76**: 14, 1938.

Sulfadiazine powder was then applied to the ulcer twice daily for eight days, with complete corneal healing. When the patient was discharged to duty there was a distinct central corneal scar, vision had improved to 20/50 in this eye. There was no recurrent ulceration, but the patient was seen two months later complaining of blurring and irritation, which were aggravated by exposure to glare and wind. These complaints were such as to interfere with full duty in the field, and assignment to limited duty was recommended.

CASE 4—A 25 year old white man was referred to the ophthalmologic eye clinic on Feb 19, 1943, while under treatment for his third attack of malaria. He complained of irritation, tearing and blurred vision in the right eye. There was a history of three similar episodes prior to his induction into military service. His visual acuity was 20/50 in the right eye and 20/20 in the left. An arborescent superficial scar involved the central and the temporal portion of the right cornea. There was a small irregular area of ulceration below the pupil. The blood smear yielded *Plasmodium vivax*. After treatment with atropine and local heat for one week the cornea was healed. On May 11, 1943 the patient suffered a fourth attack of malaria, three days later he complained again of irritation in the right eye. Examination showed a classic dendritic ulceration below the pupil. There were, in addition, a number of discrete elevated staining points, which consisted of small epithelial excrencences giving the appearance of filamentary keratitis.

On this occasion the eye was treated with sulfanilamide powder twice daily for five days, with only slight improvement. Therapy was then changed to local applications of sulfadiazine powder, and there was complete healing of the lesion in nine days. With vision impaired to 20/50 in the right eye, the patient was recommended for assignment to limited duty.

CASE 5—A 22 year old white man was admitted to the hospital on Jan 14, 1943 complaining of redness, irritation and severe photophobia in the left eye. The onset of the ocular complaint occurred two weeks prior to his admission and followed shortly an acute attack of malaria. There was no history of injury. The visual acuity was 20/20 in the right eye and 20/200 in the left. There was an irregular band of dendritic ulceration extending diagonally across the pupillary area. The blood smear yielded *Plasmodium vivax*. The patient showed no improvement when treated for two weeks with atropine and local heat. Strong solution of iodine U S P was applied on two occasions without apparent benefit. Sulfanilamide powder was used twice daily for eight days with no improvement. The eye was then treated with sulfadiazine powder, and there was complete healing of the ulcer in eight days. During four months' observation, this patient had two more acute attacks of malaria, despite intensive courses of malarial therapy. With each attack of fever there was a reactivation of the keratitis. On the first occasion discrete superficial punctate lesions appeared in previously normal areas of the cornea, while with the second malarial attack there was a marked dendritic extension from the original site of ulceration. The vision in the affected eye remained 20/200, and the patient was recommended for assignment to limited duty.

CASE 6—A 20 year old white man was admitted to the hospital on March 17, 1943 with his fourth attack of malaria and a complaint of redness, burning and tearing in the left eye. There was no history of a similar ocular complaint or of injury. The patient's vision was 20/20 in the right eye and 20/30 in the left. Examination disclosed a superficial ulceration of den-

dritic contour occupying the temporal inferior quadrant of the left eye. The blood smear yielded *Plasmodium vivax*. A cutaneous test with herpes simplex antigen gave strongly positive results. The patient's blood serum showed antibodies capable of protecting the chorioallantoic egg membrane against approximately 100,000 infectious units of known herpes simplex virus.

Instillations of 0.25 per cent zinc sulfate solution and mercury bichloride ointment 1:3,000 were used for two days without effect. Sulfanilamide powder was applied to the ulcer twice daily for six days with no improvement. The ulceration was then treated with strong iodine solution, with complete healing in six days. There was no recurrence of corneal erosion, and vision had improved to 20/20 when the patient was discharged to full duty. There had been no recurrence of keratitis after five months.

CASE 7—A 24 year old white man was admitted to the hospital on Feb 26, 1943 with his first attack of acute malaria. Four days later he noticed irritation, tearing and photophobia in the right eye. One year previously he had had a similar ocular complaint, which was not associated with malarial fever. His visual acuity was 20/30 in the right eye and 20/20 in the left. Examination showed a superficial corneal ulceration of dendritic pattern involving the inferior quadrant of the right eye. *Plasmodium vivax* was present in the blood smear. The ulcer was treated with strong solution of iodine and healed in three days, only to recur after one week. A second application of iodine to the recurrent ulceration was of no apparent benefit. Sulfadiazine powder was then applied to the ulcer twice daily for ten days, but without improvement. The lesion finally healed after two weeks' further treatment with 0.25 per cent zinc sulfate solution and mercury bichloride ointment 1:3,000. Vision in the affected eye remained 20/30. Despite having completed an intensive course of malarial therapy, the patient had a recurrent attack of acute malarial fever six weeks after admission.

Because of persisting irritation in the left eye aggravated by recurrent malaria, the patient was recommended for assignment to limited duty.

CASE 8—A 22 year old white man was admitted to the hospital March 31, 1943 with his fourth attack of malaria. On the following day he noticed increasing irritation and tearing in the left eye. There was no history of injury, and the patient had had no previous ocular disorder. His visual acuity was 20/20 in the right eye and 20/20 in the left. Examination disclosed a dendritic ulceration involving the inferior quadrant of the left cornea and extending to the border of the pupillary area. A blood smear yielded *Plasmodium vivax*. A cutaneous test with herpes simplex antigen gave strongly positive results, and the patient's blood was found to contain antibodies capable of protecting the chorioallantoic membrane against 100,000 infectious units of known herpes simplex virus. The eye was treated with strong solution of iodine, with healing of the ulcer in four days, but epithelial erosions recurred at the site of the original lesion. To this secondary ulceration sulfadiazine powder was applied twice daily for three days without improvement. Administration of the drug was discontinued, as the patient was transferred for disciplinary action, and the exact date of healing was not known. Irritation subsided in about one week, and when the patient was examined one month later the cornea was completely healed. Vision was 20/20 in each eye, and the patient was performing full field duty without complaints. There had been no recurrence of keratitis after five months.

CASE 9.—An 18 year old white youth was admitted to the hospital with his second attack of malaria on Aug 9, 1943. Two days later he noticed increasing redness and irritation of the left eye. There was no history of injury or of previous ocular complaint. His vision was 20/20 in the right eye and 20/30 in the left. Examination showed a superficial dendritic ulcer in the temporal inferior quadrant of the left cornea, encroaching on the pupillary area. *Plasmodium vivax* was present in the blood smear. A cutaneous test with herpes simplex antigen gave strongly positive results. Serum from the patient showed antibodies capable of protecting the chorioallantoic membrane against 100,000 infectious units of known herpes simplex virus. Curettings from the ulcer were transferred to a rabbit's cornea, where typical herpetic keratitis was apparent in forty-eight hours. After the initial curettage the patient was given atropine and local heat, and the cornea was healed in six days. However, two days later a small circular ulcer appeared at the original site. This ulcer was treated with sulfanilamide powder twice daily for seven days without improvement. Sulfadiazine powder was given in like manner for nine days with no benefit. The residual ulcer was then treated with strong iodine solution and healed in three days, but superficial erosions again recurred. Because of persistent irritation and failure of the cornea to heal permanently, the patient was evacuated after two months' treatment. The vision in the affected eye was reduced to 20/70.

CASE 10.—A 22 year old white man was admitted to the hospital on July 29, 1943 with his sixth attack of malaria. Five days later he noticed redness and irritation in the left eye. He gave a history of a similar episode of inflammation in this eye, which was associated with his first attack of malaria, ten months prior to his admission to the hospital. His visual acuity was 20/20 in the right eye and 20/200 in the left. Examination showed a band of dendritic ulceration extending from the upper limbus across the pupillary area, where it was continuous with a fascicle of vascularized superficial scar tissue running to the limbus below. A blood smear yielded *Plasmodium vivax*. A cutaneous test with herpes simplex antigen gave strongly positive results. Serum from the patient showed antibodies capable of protecting the chorioallantoic membrane against 100,000 infectious units of known herpes simplex virus. After the initial curettage the cornea was treated with sulfanilamide powder twice daily for ten days with no appreciable improvement. Curettings from the residual dendritiform ulcer were transferred to a rabbit's cornea. This resulted in establishment of typical herpetic keratitis. A more extensive curettage was then effected and sulfanilamide employed as before, the cornea healing in three days. However, a small circular erosion appeared after five days, and this lesion failed to respond to the powdered sulfanilamide. This secondary ulcer was finally curedtted and healed in two days, but again there was a recurrence of epithelial erosion. Sulfadiazine powder was then employed twice daily for fourteen days, without benefit. After two months' treatment the patient was evacuated because of persisting irritation and impaired vision. At the time of transfer the visual acuity in the affected eye had improved to 20/50.

RESULTS OF TREATMENT WITH SULFADIAZINE

In 3 cases (cases 1, 2 and 3) there was prompt improvement with the use of sulfadiazine powder alone, the ulcers healing completely in six to fourteen days. In case 4, in which sulfanilamide

had first been administered without apparent effect, the ulcer healed with nine days of local treatment with sulfadiazine. In case 5 sulfanilamide powder given for eight days was without effect, and two applications of strong iodine solution failed to result in complete healing. This ulcer finally healed solidly after eight days' local therapy with sulfadiazine. In case 7 a recurrent ulceration was treated with sulfadiazine for ten days without improvement. The ulcer in case 8 was treated with iodine and healed in three days, only to recur subsequently. This secondary erosion was treated with sulfadiazine for three days without apparent benefit. In case 9 a recurrent ulcer failed to heal after nine days' local therapy with sulfadiazine, and in case 10 a similar lesion showed no improvement after fourteen days' employment of the drug.

Thus in the 5 cases of ulcers of dendritic pattern, sulfadiazine was apparently helpful. However, there was no appreciable benefit which could be attributed to sulfadiazine in 4 cases of recurrent corneal ulcerations of the metaherpetic type.

RESULTS OF TREATMENT WITH SULFANILAMIDE

In cases 4, 5 and 6 the sulfanilamide powder was found to be of no benefit in treating fresh dendritic ulcers. In case 9 a recurrent ulceration was treated for seven days without apparent improvement. In case 10 sulfanilamide was apparently of no value even when combined with curettage. In this instance it was possible to demonstrate the presence of herpes simplex virus in the residual dendritic lesion after ten days' treatment with the powdered drug.

HERPES SIMPLEX KERATITIS AS A FACTOR INCAPACITATING TROOPS FOR FULL DUTY

Only in corneal infections does herpes simplex result in permanent scarring. The number of patients requiring assignment to limited duty because of impaired vision is notoriously high after attacks of dendritic keratitis, particularly when early and energetic treatment is not available. There is also the problem of ulceration recurring with subsequent attacks of malaria. Even without active erosion of the epithelium, the eye often remains irritable and sensitive to wind and glare for a long period.

In addition to the 13 patients with dendritic keratitis considered in determining the incidence among new patients coming to the clinic from malarial and nonmalarial groups, 7 patients with

active or recently healed superficial herpes simplex keratitis were transferred to this hospital from other areas. There were also 2 patients with nonspecific deep keratitis that was probably of the same causation. Of these 22 patients with dendritic keratitis, 15 could not be discharged to full duty and each of the 2 patients with deep keratitis of probable herpetic causation required evacuation. Table 2 shows the relative incidence of herpetic keratitis as a factor in restricting disposition of patients to full duty.

TABLE 2.—Relative Incidence of *Herpes Simplex* Keratitis as Cause for Disposition to Limited Duty

	No Cases
Herpes simplex keratitis superficial	15
Deep keratitis, probably herpetic	2
Sclerokeratitis	1
Interstitial keratitis, syphilitic	1
Trachoma	1
Inflammation of iris or choroid and retina	12
Ocular injuries	12

As may be seen, keratitis associated with herpes simplex necessitated more dispositions to limited service at this station during this period than any other single inflammatory lesion of the eye and also more than did ocular injuries.

LABORATORY TESTS

Transference of the Infection to the Cornea of Rabbits—From a cornea of each of 2 patients with dendritic keratitis occurring in conjunction with acute malaria the virus of herpes simplex was isolated (cases 9 and 10). By the method described by Gruter,²¹ scrapings were transferred directly to a cornea of a rabbit. In each instance typical herpetic keratitis was produced, and it was possible to transfer the infection to a cornea of a second rabbit.

Unfiltered exudate from the conjunctival cul-de-sac of the rabbit was then inoculated onto the chorioallantoic membrane of a 12 day chick embryo, according to the technic of Burnet.²⁶ The lesions produced were identical with those caused by a known strain (HFE) of herpes simplex virus.

To prove conclusively that the keratitis in the rabbits was due to herpes simplex virus, neutralization tests were carried out on successive samples of each animal serum. The first sample of blood was withdrawn at the time of the initial corneal infection. After inactivation at 56°C. for thirty minutes the serum was preserved at 4°C. A second specimen was taken after three weeks and was similarly treated. Simultaneous neutralization tests were then carried out according to the following technic:

A suspension of a known strain (HFE) of herpes simplex virus was used, containing approximately 100,000 infectious units as shown by a previous titration. This was added to an equal volume of the affected rabbit's serum, and 0.05 cc. of the mixture was then inoculated onto the chorioallantoic membrane of a 12 day

chick embryo. After three days' incubation the eggs were examined. Serum from the first specimen taken at the time of the initial infection had failed to neutralize the virus. These membranes showed characteristic semi-confluent herpetic lesions, and in most instances the embryos were dead. However, the serum obtained three weeks after the initial infection completely neutralized the suspension of known herpes virus inasmuch as all embryos were living and there were no lesions due to the virus on the chorioallantoic membranes. It was therefore concluded that the causative agent which was isolated from the human cornea and was transferred to the rabbit's cornea and then to the chorioallantoic membrane of a 12 day chick embryo was herpes simplex virus.

Similar neutralization tests were carried out on the sera of 10 patients with active or recently healed dendritic keratitis. In each patient's serum antibodies were present which were capable of protecting the chorioallantoic membrane against about 100,000 infectious units of a suspension of known herpes simplex virus.

CUTANEOUS TEST FOR HERPES SIMPLEX INFECTION

Nagle²⁷ has described a specific cutaneous reaction present in persons infected with the virus of herpes simplex. He found a close correlation between positive cutaneous responses and presence of serum antibodies. It has been generally assumed that demonstration of serum antibodies is conclusive proof of past or present herpetic infection. Gallardo²⁸ has demonstrated, however, that absence of serum antibodies can occur during the first eighteen days of a keratitis which constitutes the primary lesion due to herpes simplex.

The herpes simplex antigen used in the cutaneous test consisted of heat-killed virus prepared from chorioallantoic membrane infected with the HFE strain of herpes simplex. The control was prepared from normal chorioallantois in a similar manner. An intradermal injection of 0.10 cc. was given, as in tuberculin tests, and readings were made after twenty-four hours.

The skin of 13 patients with active or recently healed herpetic keratitis was tested and in every instance found to give a strongly positive response to the antigen. Each of these patients had previously been shown by neutralization tests to have herpes simplex antibodies in the serum. Burnet and his associates²⁹ have re-

27 Nagler, F P O. A Specific Skin Reaction in Persons Infected with the Virus of Herpes Simplex to be published.

28 Gallardo, E G. Primary Herpes Simplex Keratitis. Clinical and Experimental Study, Arch Ophth 30:217 (Aug) 1943.

29 (a) Burnet, F M., and Williams, S W. Herpes Simplex. New Point of View, M J Australia 1:637, 1939. (b) Burnet, F M., and Lush, D. Herpes Simplex Studies on Antibody Content of Human Sera. Lancet 629, 1939.

26 Burnet F M. The Use of the Developing Egg in Virus Research, Medical Research Council, Special Report Series, no 220, London, His Majesty's Stationery Office 1936.

ported antibodies for herpes simplex virus present in as high as 90 per cent of adults. Using the cutaneous test, Nagler²⁷ found 80 per cent positive reactions among the older age groups. As a check on the incidence of positive cutaneous reactions in this hospital, the skin of 148 patients was tested as a sample. Of this total, 64 had had malaria and 84 gave no history of the disease. The incidence of positive cutaneous reactions was 78.1 per cent in the malarial group and 80.9 per cent in the nonmalarial group. The significance of a positive cutaneous reaction as an aid in the diagnosis of atypical keratitis in adults is therefore negligible, but a negative cutaneous reaction might prove valuable in ruling out herpetic infection of appreciable duration. Nagler,²⁷ however, in testing infants and young children found that the incidence of positive cutaneous reactions is less than 20 per cent in the first four years of life. Burnet and Lush^{29b} have made this same observation on the basis of determinations of serum antibody, using the chorioallantois. The age distribution is likewise in accord with the following figures, quoted by Weyer,³⁰ for positive findings as to the presence of serum antibody: 0-5 years, 14 per cent; 5-10 years, 38 per cent. As Gundersen¹² has pointed out, it is this period, the first five years of life, that also has the highest incidence of dendritic keratitis. He further states that in young children herpetic keratitis is frequently mistaken for interstitial keratitis or phlyctenulosis. In such cases an easily repeated cutaneous test could prove of value, particularly when detailed examination is difficult and extensive laboratory facilities are not available.

SUMMARY AND CONCLUSIONS

There appears to be an increased incidence of keratitis associated with herpes simplex in a population heavily infected with malaria. Among new patients at the ophthalmologic clinic studied during an eighteen month period, there have been more than six times as many from a malarial division as from a comparable group that had not been exposed to malaria. However, less than 0.2 per cent of patients with acute malaria admitted to the general medical service of this hospital ever had this type of herpetic keratitis. Hence the likelihood of precipitating a dendritic

ulcer in the individual patient with therapeutic malaria would seem very small.

Early diagnosis and intensive treatment of the malarial fever are essential in the management of herpetic keratitis occurring in patients with malaria. Recurrent attacks of malaria are often associated with a reactivation or an extension of the corneal ulceration.

Through impairment of vision and prolonged irritation of the eye herpes simplex keratitis has necessitated more disposition to limited duty of patients at this station than any other single eye condition.

Sulfadiazine powder applied locally to 5 dendritic ulcers seemed to promote rapid healing in each instance. In 4 cases of atypical recurrent herpetic ulcers sulfadiazine was of no demonstrable benefit. These results suggest that sulfadiazine may prove a satisfactory adjunct to the accepted treatment of dendritic keratitis with strong solution of iodine U.S.P.

Local applications of sulfanilamide were of no apparent value. In 3 patients with ulcers of dendritic pattern and in 1 patient with recurrent ulceration no improvement resulted. The herpes simplex virus was isolated from 1 dendritic ulcer after ten days' treatment with the drug.

From the cornea of each of 2 patients with recurrent malarial attacks and dendritic keratitis the causative agent was transferred to a rabbit's cornea and thence to the chorioallantoic membrane of a chick embryo, where characteristic lesions of herpes simplex virus were produced. The identity of the virus was confirmed by neutralization tests.

When the skin was tested for sensitivity to herpes simplex antigen positive responses were obtained in about 80 per cent of a sample of hospitalized adult patients, and there was no appreciable difference in incidence between malarial and nonmalarial patients.

Thirteen patients with herpes simplex keratitis were shown by neutralization tests to have serum antibodies against a known strain of herpes simplex virus. Each of these patients gave a strongly positive cutaneous reaction to the herpes simplex antigen.

The possible value of such a cutaneous test in certain atypical cases of herpetic keratitis has been indicated.

We received advice regarding this work from Dr F. M. Burnet. Dr Burnet also made available the laboratory facilities of the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne, Australia.

²⁹ Weyer, E. R. Herpes Antiviral Substances Distribution in Various Age Groups and Apparent Absence in Individuals Susceptible to Poliomyelitis, Proc Soc Exper Biol & Med 30: 309, 1932.

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TOXOPLASMOSIS

REPORT OF OCULAR FINDINGS IN INFANT TWINS

PARKER HEATH, MD
AND
WOLFGANG W ZUELZER, MD
DETROIT

Toxoplasmosis is a recently recognized infectious disease in human beings. Four principal types have been reported: (1) a granulomatous encephalitis, usually of congenital origin and occurring in fetal or early infantile life; (2) an acquired acute encephalitis occurring in children; (3) an acquired acute disease resembling Rocky Mountain spotted fever occurring in adults; (4) a latent subclinical form occurring in adults.

Sabin, in 1943,¹ outlined the status of Toxoplasma, which was isolated by Nicolle and Manceaux from the gondi North African rodent in 1908² and by Splendore from the rabbit in Brazil in the same year. The parasite has been classified as a protozoon of the genus Toxoplasma. It has a wide geographic distribution and occurs in many species of animals, both wild and domestic. Sabin and Olitsky in 1937³ found the parasite in guinea pigs and were able to transmit it through several animal passages. The morphologic characteristics of Toxoplasma have now been well established by Perrin⁴ and the features of the experimental disease have been studied adequately by Levaditi⁵, Sabin⁶ and

Wolf, Cowen and Paige.⁷ Little is known about the life cycle of Toxoplasma, the natural mode of transmission and the epidemiology of human toxoplasmosis.

In infants the central nervous system is especially susceptible to toxoplasmic infection. The principal clinical findings are internal hydrocephalus or microcephaly, roentgenographic evidence of focal cerebral calcifications and bilateral chorioconjunctivitis, which attacks particularly the area centralis. Convulsions are commonly noted. The spinal fluid in the active stage of the disease shows an increase in protein content, pleocytosis and xanthochromia. Additional diagnostic evidence may be obtained by demonstration of neutralizing antibodies against Toxoplasma in the serum of the patient. The technic was developed by Sabin⁸ and consists in mixing varying dilutions of the patient's serum with a suspension of mouse brain containing the parasites and injecting the mixture intracutaneously into rabbits. The local reaction is compared with that produced by a similar mixture containing control serum from a normal person. The test is difficult to perform and even more difficult to interpret, but in trained hands it has given reliable results. In some cases it has been possible to transmit the disease to animals by inoculation of spinal fluid or tissues intracerebrally or intraperitoneally. The pathologic lesion in the central nervous system consists of necrosis followed by calcification and by a tendency to form granulomas. Miliary granulomas with epithelioid cells, focal meningeal and cerebral inflammatory areas with

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1 Sabin, A. B. Toxoplasmosis, in Brennemann, J. Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1943, vol. 4, pp. 43-54.

2 Nicolle, C., and Manceaux, L. Sur un protozoaire nouveau du Gondi, Compt. rend. Acad. d. sc. **148** 369-372, 1909, Toxoplasma, Arch. Inst. Pasteur de Tunis **2** 97, 1909.

3 Sabin, A. B. and Olitsky, P. K. Toxoplasma and Obligate Intracellular Parasitism. Science **85** 336-338 (April 2) 1937.

4 Perrin, T. L. Toxoplasma and Encephalitozoon in Spontaneous and in Experimental Infections of Animals, Arch. Path. **36** 568-578 (Dec.) 1943.

5 Levaditi, C. Au sujet de certaines protozooses hereditaires humaines à localisations oculaire et nerveuse, Compt. rend. Soc. de Biol. **98** 297-299, 1928.

6 Sabin, A. B. Toxoplasmic Encephalitis in Children, J. A. M. A. **116** 801-807 (March 1) 1941.

7 Wolf, A., Cowen, D., and Paige, B. H. (a) Human Toxoplasmosis. Occurrence in Infants as an Encephalomyelitis, Verification by Transmission to Animals, Science **89** 226-227 (March 10) 1939, (b) Toxoplasmic Encephalomyelitis III. A New Case of Granulomatous Encephalomyelitis Due to a Protozoon, Am. J. Path. **15** 657-694 (Nov.) 1939.

8 (a) Sabin, A. B., and Ruchman, I. Characteristics of the Toxoplasma Neutralizing Antibody, Proc. Soc. Exper. Biol. & Med. **51** 1-6 (Oct.) 1942 (b) Sabin, A. B. Toxoplasma Neutralizing Antibody in Human Beings and Morbid Conditions Associated with It, ibid. **51** 6-10 (Oct.) 1942.

lymphocytes, plasma cells, glial cells, large mononuclear cells, histiocytes, eosinophils and some capillary hypertrophy and conglomerate foci of necrosis, ranging from microscopic dimensions to several centimeters in size, are scattered through the hemisphere and into the white matter, cavities may be formed, parasites, intracellular and

which are often seen in the basal ganglia. Internal hydrocephalus and large areas of cortical atrophy are commonly noted. Steiner and Kaump,¹⁰ in a recent report on the pathologic changes in an infant, expressed the opinion that the lesions are pathognomonic. The ocular changes have been studied by Koch, Wolf,

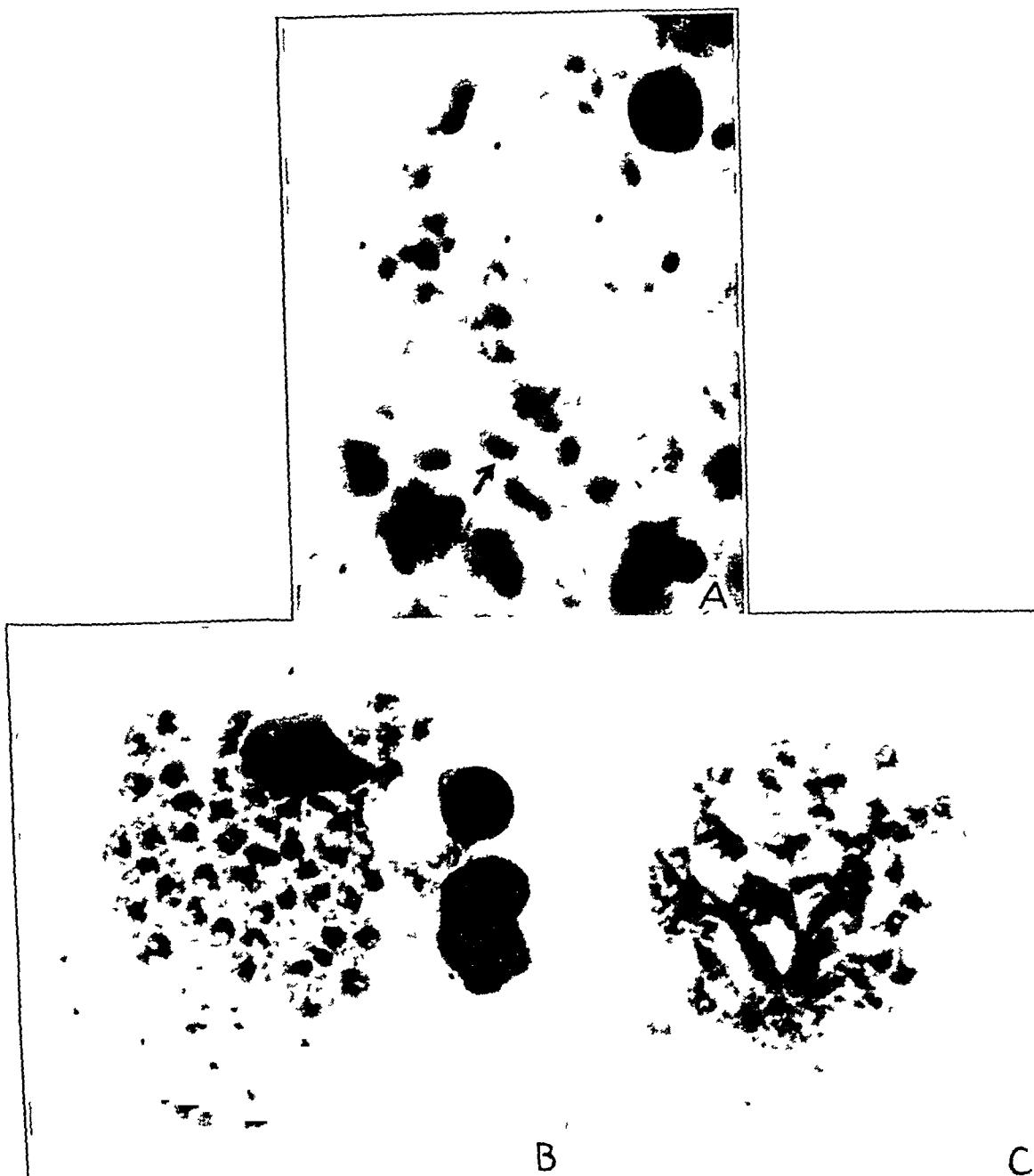


Fig 1 (from Sabin¹)—A, toxoplasmas in tissue after fixation in a dilute concentration of solution of formaldehyde U S P Hematoxylin and eosin stain, $\times 1,400$ B, intracellular aggregate of toxoplasma, $\times 1,000$ C, pseudocyst, $\times 1,000$

free, may be seen in affected or clear areas. Calcium forms early and is characteristically present in older lesions.⁹ This substance appears on roentgenographic films as a few to many small rounded areas or curved lines, the latter of

Cowen and Paige¹¹. Adequate studies of the eyes in older patients were not found in the literature.

¹⁰ Steiner, G., and Kaump, D. H. Infantile Toxoplasmic Encephalitis, *J. Neuropath. & Exper. Neurol.* 3: 36-48 (Jan.) 1944.

¹¹ Koch, F. L. P., Wolf, A., Cowen, D., and Paige, B. H. Toxoplasmic Encephalomyelitis. VIII. Significance of Roentgenographic Findings in the Diagnosis of Infantile or Congenital Toxoplasmosis, *Am. J. Roentgenol.* 47: 830-841 (June) 1942.

SUMMARY OF CASE HISTORIES¹²

CASE 1—*History*—H, a Negro premature infant and one of identical twins, was born on Sept 5, 1943 and admitted to Children's Hospital half an hour after birth

The mother had been in good health during pregnancy but during the last three months had complained of anorexia, attacks of dizziness and blurring of vision. Her blood pressure was said to have been normal. The expected date of confinement was October 17. There was no known cause for the premature onset of labor. The mother had not been aware that she was carrying twins. She had thought that the fetus had been unusually quiet during the last few months. She had two older children, aged 4 and 2 years, both of whom were in good health.

The father was likewise healthy. The family had come to Detroit in 1940 from the state of Mississippi. The father was a municipal employee, whose work consisted of collecting refuse. In the performance of his duties he had to handle dead rats, as well as to catch live ones. The family lived in a five room framework house in the Negro section of Detroit. They kept no pet animals, and the mother recalled no intimate contact with animals at any time. However, the house had been infested by mice at various times.

The patient was born by frank breech delivery five minutes after the other twin. He was extracted with difficulty and had to be stimulated in order to breathe and cry properly. Nevertheless, he had satisfactory color when he was admitted to the hospital.

Examination—Physical examination revealed a well developed but somewhat inactive premature infant, weighing 3 pounds and 11 ounces (1,619 Gm). The skin was covered with orange vernix caseosa. The cranial sutures were widely separated, but the fontanelles did not appear to be under abnormal tension. The remainder of the findings were noncontributory. The laboratory data obtained on the child's admission to the hospital were likewise not unusual. The Kline test gave negative results.

Röntgenograms revealed slight enlargement of the heart and adequate aeration of the lungs. In the long bones, multiple transverse bands of increased density were noted near the metaphyses. The skull was not examined.

Course—The patient received the usual care for premature infants. On the third day icterus of the skin and scleras was noted. There was also a transient fine punctate rash over the entire body. The icterus persisted, and abdominal distention developed. The stools became clay colored. The temperature was unstable at first often subnormal and later febrile. There were repeated attacks of cyanosis. During one of these attacks the child died, at the age of 1 month.

Pathologic Study—A complete autopsy was performed twelve hours after death. The pertinent gross somatic changes of significance were generalized icterus and enlargement of the liver and spleen. The brain presented a striking appearance, with numerous bright yellow lesions of varying size on the surface of the hemispheres. There was a severe degree of internal hydrocephalus. On the cut surface numerous cavities were noted. These were filled with gritty or friable

yellow or white material, had irregular contours and often measured several centimeters in diameter. Similar yellowish material was present in the lining of the lateral ventricles.

Microscopically the cerebral lesions consisted of large areas of necrosis and calcification, which were often surrounded by granulation tissues composed of fibroblasts, histiocytes, giant cells, plasma cells and rare eosinophils. There were large, bandlike areas of calcification in the walls of the ventricles. The ependymal lining was largely destroyed and covered by glial proliferations. The vessels were surrounded by collars of inflammatory cells, in many areas, notably in the brain stem and the spinal cord, miliary granulomas were seen. These consisted of inflammatory cells, mainly mononuclear cells and glial elements. Parasites with the characteristic appearance of toxoplasmas were present in round, cystlike aggregates in apparently normal tissue but were seldom noted in areas of severe inflammatory reaction, necrosis or calcification.

The liver was the seat of diffuse, severe degenerative changes. There was fairly extensive extramedullary hemopoiesis in the liver, spleen and other organs. No parasites were found outside the brain, spinal cord and retina.

The right eye was removed and fixed entire in Zenker's solution, no gross abnormality was noted. The size was smaller than is normal for a full term baby. The corneal curve was less differentiated, more like that of an eye in a 7 month fetus. The sclera was a good deal thinner than the cornea, but episclera could be well distinguished. The angle of the anterior chamber was shallow, the mesoderm in the angle was not entirely atrophic (as it should be by the eighth month), and the remnants were abnormally cellular. Schlemm's canal was situated deep in the angle (fetal). The scleral spur, also, was behind the angle, as it should be into the seventh month. Red cells were in the anterior chamber. The major circle of the iris lay well behind the angle (In an adult it is only slightly behind or on a level with it). The sphincteric portion of the musculature of the iris was well developed (fourth month). The pupillary area showed a persistent vascular blood-containing fetal membrane and partly inflammatory remnants, some of which were attached to the capsule of the lens, as seen in fetal iritis. The stroma of the iris was loose, edematous and negroid. Increased pigment was noted in the anterior portion of the stroma, due to migration from a deep layer. The two pigment layers of the retina were edematous. The ciliary body was loose edematous and well developed with meridional muscle fibers, unlike the not clearly differentiated circular fibers (as should be the case in the seventh month). The ciliary processes were well developed, were loose and open and showed dissociation of pigment, plasma cell infiltration and a few nucleated erythrocytes. On the surface of the processes were noted a few plasma cells and monocytes, considerable tertiary vitreous and condensation of the *faisceau isthymique* and clumps of pigment. The pars plana was well developed, and the ora serrata was well behind the ciliary body. The conjunctiva near the limbus showed a few small foci of perivascular lymphocytes. The extraocular muscles at their attachment to the globe showed a few thin foci of lymphocytes and plasma cells. The lens, which was round, showed the epithelium of the anterior and posterior surfaces to be well developed. No retrolental

12 A full report on these 2 cases will be given in a separate article, which is now being prepared by one of us.

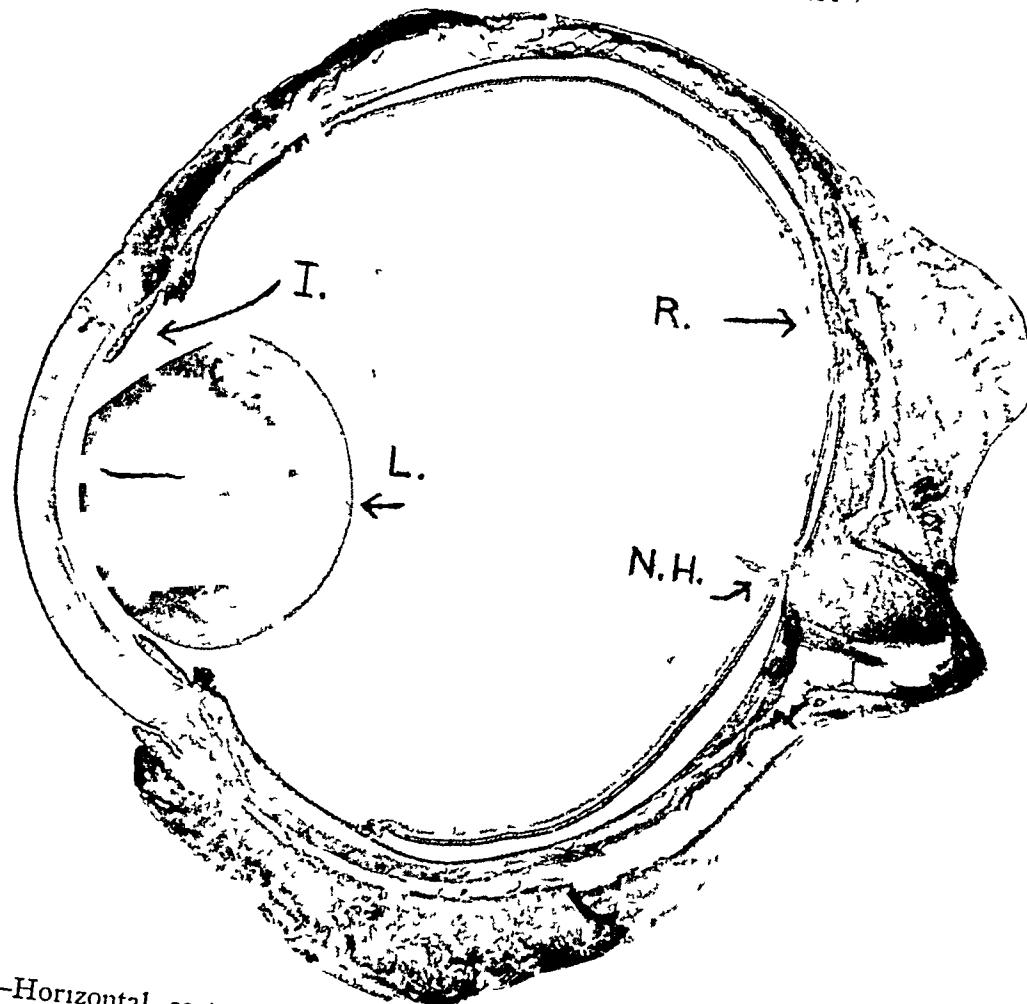


Fig 2 (Case 1)—Horizontal section of the right eye *I*, fetal iris and angle, *L*, fetal lens, *NH*, optic nerve head with persistent hyaloid artery, *R*, chorioretinal lesion



Fig 3—Details of the iris *C*, cornea, *I*, iris, *VM*, vascular membrane, *L*, lens with remnant of adhesion

vessels were seen. The vitreous was coarsely fibrillar and contained a few cells—mostly large mononuclears.

The choroid was well differentiated but more cellular than that of an adult. It showed extensive involvement, with rather sharply bordered destructive granulomatous lesions accompanying the retinal foci. Edema was severe and dissociation of structure, migration of pigment and extensive venous congestion (vessels contained nucleated red cells) were present, capillary hyperplasia and vascular proliferation were not significant. The retina was for the most part artefactitiously separated but showed areas of subretinal hemorrhage. The granular layers were well developed, and the outer showed few oval nuclei. Cones and rods were partly destroyed in areas and associated with hemorrhage and appeared ill formed (partly due to fixation and processing). The granular layers were not so compact as in the adult state. The ganglion cell layer was poorly represented. The pigment layer of the retina was of a heavy negroid type. Muller's fibers were greatly exaggerated and hyperplastic in the inner layers, which were not fully differentiated and showed new connective tissue. The nerve fiber layer was loose, wide and disarranged. A few plasma cells, lymphocytes and mononuclear cells had infiltrated, and histiocytes, storing pigment and debris, were noted. An occasional cystlike aggregate of toxoplasmas was seen in the inner nuclear layer, and not in the severe destructive granulomatous areas in the retina. One cluster was observed at the level of the nerve fiber layer. Inflammatory foci were mostly retinal and gave the impression that this layer was the point of origin. The macular area was occupied by a large, swollen necrotizing lesion. Plasma cells were noted in moderate abundance, as well as a few lymphocytes. The necrotizing retinal lesion showed disintegrating cells, some of which had been flung into the vitreous—dissociation and migration of pigment were pronounced as one proceeded inward. Hemorrhage was noted on the surface of the retina. No parasites were seen in the necrotizing lesion.

The optic nerve in longitudinal section showed persistence of the hyaloid artery, extending partly into the vitreous. The lamina cribrosa was less compact than in the adult eye and proceeded straight across the scleral opening. Edema bordered the central vessel meniscus, and the nerve head was likewise edematous, no foci were noted in the optic nerve substance. The leptomeninges showed foci of lymphocyte infiltration. A physiologic cup was not present. The vaginal space was open.

In general except in the area centralis the cells and tissue layers of the retina of a 7 month old human fetus are arranged like those of the retina of an adult. This was true in the case presented. The impression was that the inflammatory process was unusually severe, selective and discrete and had not had time for repair. The pigment had not collected in depots, and no fixed scar had evolved. No calcium was noted in the retina or the choroid.

CASE 2—L. H., the identical twin of the preceding patient, was likewise born by frank breech delivery but was in good condition immediately on birth and was the larger of the twins.

On admission to the hospital he weighed 5 pounds and 8 ounces (2,494.8 Gm.). He was somewhat inactive but responded well to external stimuli. There was a mild degree of separation of the cranial sutures. Otherwise the patient appeared to be a normal prema-

ture infant. The laboratory data on admission were noncontributory.

Course—Like his brother, the patient became icteric at the age of 3 days. For two weeks he had a purulent discharge from the umbilicus. He received sulfadiazine by mouth. Although listless, the child ate fairly well. There were episodes of cyanosis and dyspnea. The temperature at times was elevated. Abdominal distention was noted, and the icterus persisted. Nevertheless, the child gained weight and was discharged on September 30, at the age of 25 days.

He returned one week later, October 6, because of diarrhea and symptoms of a cold. From this time on he was under almost continuous observation, either in the ward or in the outpatient department. A thorough investigation was made at the time of his first readmission to the hospital because by this time the autopsy on the twin brother had revealed toxoplasmosis.

Examination—The following pertinent data were obtained. The child was still jaundiced. The abdomen was distended, the stools were clay colored, and the urine contained bile. The hemoglobin content of the blood was 15 Gm per hundred cubic centimeters. The white blood cell count was 8,800. The spinal fluid was xanthochromic and contained 500 red cells and 20 white cells per cubic millimeter. The protein content was greatly increased. Neurologic symptoms were absent, and no abnormal physical characteristics were observed in this respect. Roentgenograms of the skull revealed multiple small areas of intracerebral calcification. Later, a mild degree of internal hydrocephalus was demonstrated encephalographically.

The first ophthalmologic examination (Dr. H. L. Begle) revealed uveokeratitis. The corneas were somewhat hazy, and the fundi were at first not clearly visualized. A few days later the fundi appeared diffusely gray. The optic disks were indistinct. Localized lesions were not recognized at this time, owing to cloudy media, nystagmus and difficulty of examination.

Further Course—The patient remained jaundiced until the fifth month. During most of this time the abdominal distention persisted. The liver and the spleen became palpable for a time. There were several episodes of intercurrent infections accompanied by respiratory symptoms, and on one occasion abscesses developed on both legs. One of these required surgical drainage, and hemolytic streptococci were cultured from the pus. In spite of these setbacks, the patient gained weight and kept pace with the majority of premature infants so far as physical development was concerned. Mentally he appeared slightly retarded when last seen, at the age of 7 months. At this time there was a suggestion of a tonic neck reflex and the right knee jerk was hyperactive. The spinal fluid was examined on several occasions and did not become normal until the patient was 4½ months old.

Through the permission of Dr. Joseph Heidelman, of the Wilmer Ophthalmological Institute, Johns Hopkins Hospital, the serum of each of the patients and of the mother was tested for neutralizing antibodies against the toxoplasma. The method used was essentially that described by Sabin. The serum of the dead twin was obtained at autopsy and was not processed until several days afterward. The results in this case were doubtful. The serums of both the living twin and the mother, which were processed by immediate freezing at —40 F and desiccated in a vacuum, contained neutralizing antibodies against the toxoplasma.

Ophthalmologic Examination — Ocular Findings at Eight Weeks (Dr Begle) The pupils reacted to light, vision was questionable, no fixation on objects was noted, the corneas were still hazy, threadlike extensions of the pupillary borders passed into the upper and the lower quadrant. The disks were sharp now, there were a few circumscribed lesions in the right macular area, the left pupil was undilated.

At 5 months one of us noted that the eyes were smaller than normal and showed irregular nystagmus and dissociation in movement, which was not limited. The left eye usually appeared to converge to about 30 degrees. The cornea of the right eye showed diffuse

exudative retinal lesion. A similar, much smaller, lesion was noted in the mesial half of the retina about halfway between the nerve head and the periphery. The borders were round and showed areas resembling hemorrhage, the exudative process and the loss of transparency obscured the retinal vessels.

The left eye showed decided persistence of the fetal vessels around the entire circumference and a smaller, more irregular pupil (in spite of instillation of homatropine drops). It was even more difficult to make out the details in the left fundus, but a similar retinal lesion, resembling exudative chorioretinitis over a limited area, was noted in the temporal half.

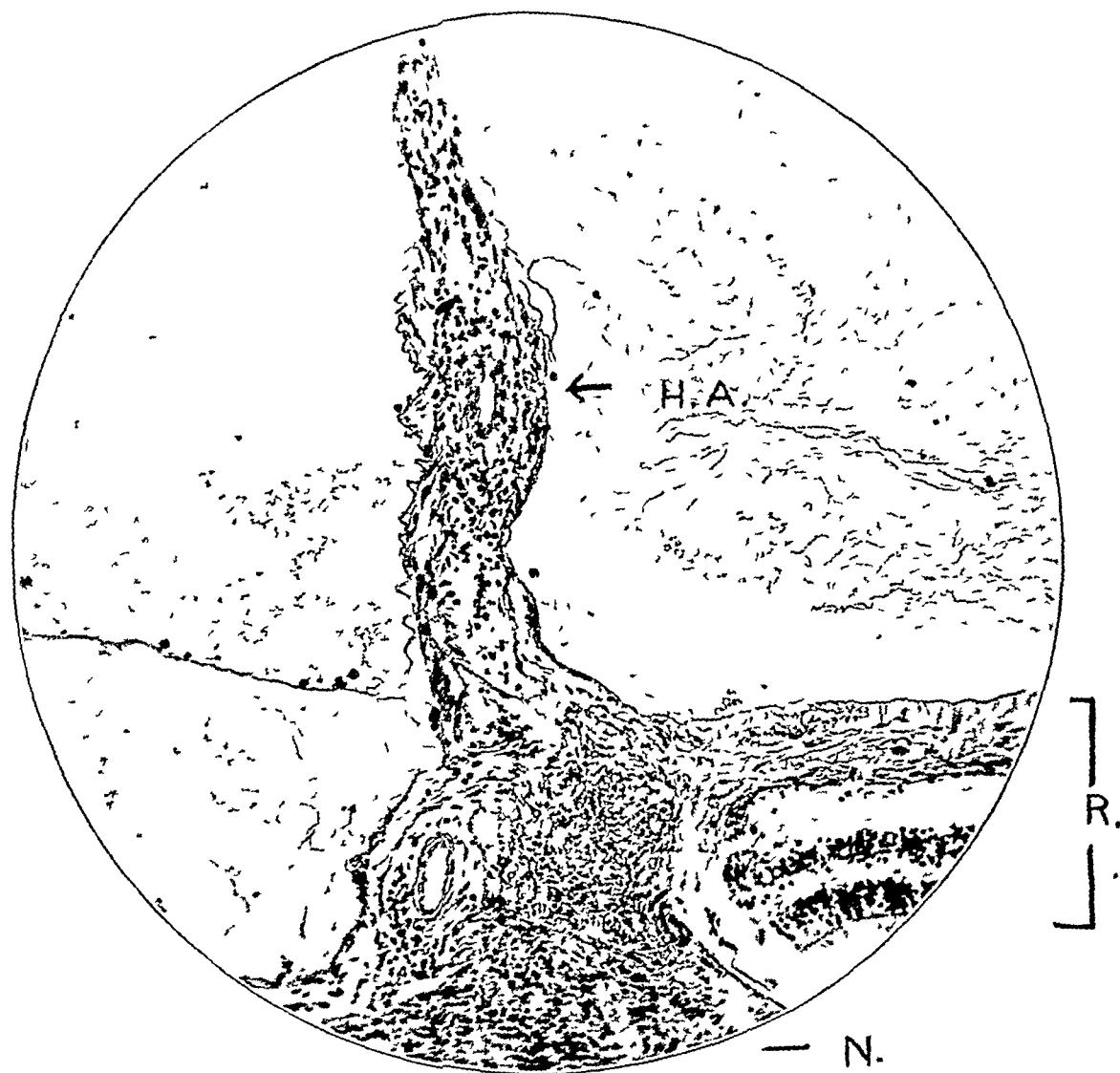


Fig 4.—Details of the optic nerve head. H.A., hyaloid artery; R., retina; N., optic nerve.

loss of normal transparency. The anterior chamber was shallow. The pupil reacted to light sluggishly. The patient was attracted toward bright light. The pupil dilated partially and unevenly under the influence of homatropine, owing to partial persistence of the pupillary membrane (especially in the down and in quadrant) and associate posterior synechia. Many vessels originated at the border of the pupil. The media showed some loss of transparency of the cornea, and the lens was apparently clear except where the anterior capsule was disturbed by the pull of the synechia. The vitreous showed diffuse haziness. The optic nerve head appeared congested and somewhat edematous, and the fine details were difficult to see. Central vessels were noted on the nerve head. On the temporal side, including more than the macula and running over to the nerve, was a slightly elevated, whitish to ivory-colored

The use of general anesthesia to permit easier examination was not thought advisable or permitted, but the use of local anesthesia, a speculum and fixation with a lock forceps proved fairly satisfactory. Intraocular pressures were estimated, by digital means, to be low normal.

In general, the impression of these early lesions was as follows. They were severe, large, exudative, elevated and ivory white, with fairly sharp and partly hemorrhagic borders, associated with a good red reflex coming through the adjacent transparent retina and with the vitreous affected only minimally.

Successive examinations of the fundi of the surviving twin have shown that a slow recession of the retinal process is in progress.

The characteristics of the early retinal changes, as illustrated in this case, were multiple bilateral large,

whitish, exudative, elevated macular lesions, which were fairly sharply bordered, sometimes with hemorrhage, and were seen through an only moderately disturbed vitreous.

OCULAR LESIONS IN CONGENITAL TOXOPLASMOSIS

Janků¹³ reported as parasitic cysts (*Sporozoa*) lesions in the retina of a hydrocephalic infant associated with macular coloboma, and in the left eye with microphthalmos. Levaditi⁵ classified Janků's parasite as the toxoplasma, and also that in a case reported by Torres

From these reports and our cases, it is evident that this disease in infants is commonly associated with microphthalmos in one or both eyes. The incidence is so high that it is reasonable to assume that the microphthalmos is inflammatory in origin. A small eye may result from uveitis, whether principally anterior or posterior. The persistent vessels seen in the pupillary areas were embryonic and were associated with inflammatory adhesions of the iris to the lens; they represented a fetal vascular persistence plus a fetal uritis. In nearly all of the reported cases

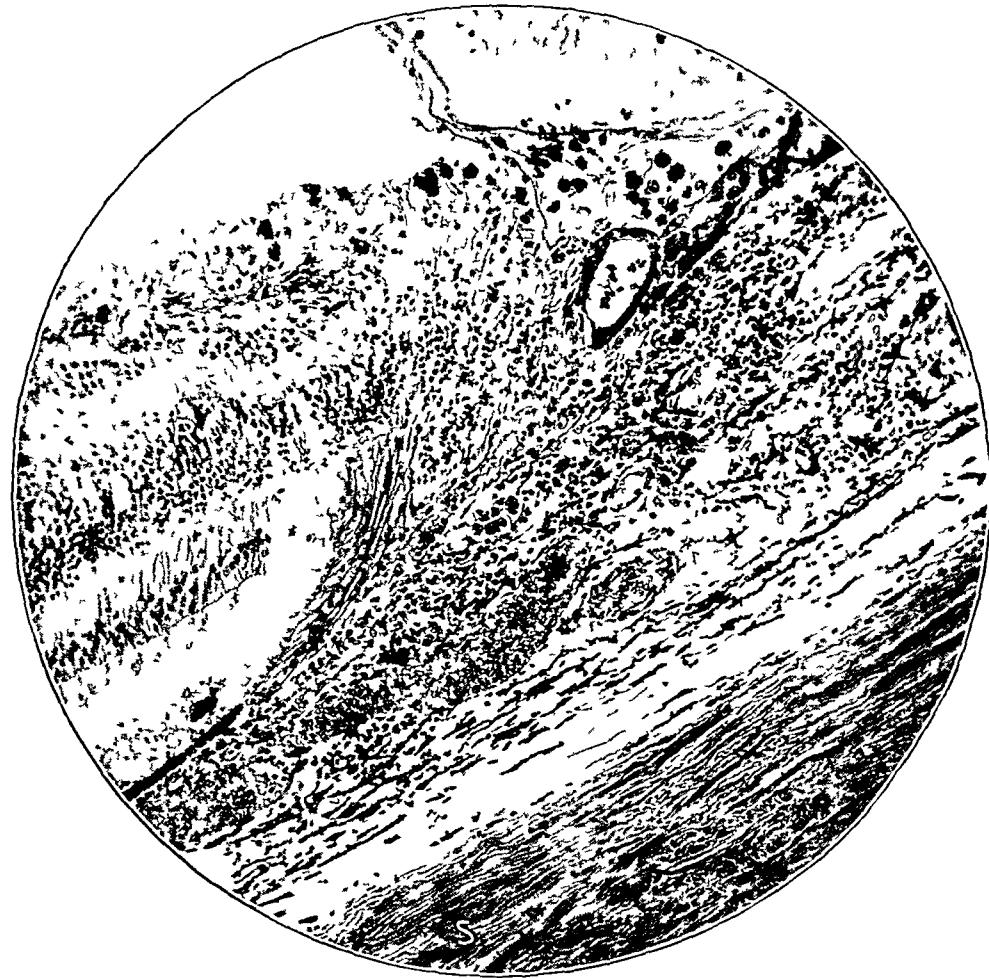


Fig 5.—Details of the border of the chorioretinal lesion. R, retina, C, choroid, S, sclera.

Vail^{8b} and co-workers studied older children and adults and related ocular lesions to positive reactions to neutralizing antibodies against the toxoplasma.

Koch, Wolf, Cowen and Paige¹¹ reviewed previously reported cases and presented interesting data concerning examinations of the fundus and histologic features of ocular lesions in the posterior segment.

¹³ Janků, J. Pathogenesis and Pathological Anatomy of Coloboma of the Macula Lutea in an Eye of Normal Dimensions and in a Microphthalmic Eye in the Retina, Časop Iek česk. 62: 1021, 1052, 1081, 1111 and 1138, 1923.

squint, irregular and searching nystagmus, sluggish reaction of the iris to light, pupillary membrane or vessels and low visual acuity were noted.

The chorioretinitis is usually bilateral in toxoplasmosis. It begins in slightly elevated areas showing in the retina loss of transparency, and soon is converted into an obvious exudative lesion, which is yellowish white, gray or darker red (dependent on age, hemorrhage and pigment) and fairly sharply bordered, with rounded contours. The multiple severe chorioretinal lesions are discrete, and the unaffected areas between as well as the vitreous are relatively

clear. This is consistent with the histologic observations, in which the lesions were seen to be rather sharply circumscribed. The size of the involved chorioretinal areas varies from small miliary to large exudative foci. Hemorrhage in the vitreous is not characteristic although opacities of the vitreous were reported in 1 case.

Severe optic neuritis is not the rule. Pigmented borders in the old lesions and over-sclera atrophy are common. The old lesions resemble colobomas and macular dysplasia. The term coloboma may properly include such inflammatory mutilations, although the term is usually applied to noninflammatory lesions.

The age of the lesion in the fundus may be estimated by the presence or absence of blood vessels and their relation to the lesion. According to Mann,¹⁴ the choioiditis of fetal life cannot have begun before the fifth month if the retinal vessels and some layers of the retina are over the patch of destruction. In cases in which the overlying retina is destroyed, together with the vessels in it, which stop abruptly at the edge of the patch, the condition may possibly have arisen during the fifth or sixth month. If the retina becomes involved in a destructive inflammation of the choroid before the disappearance of the *vasa hyaloidea propria* in the vitreous, it is possible that the lesion may have occurred by or before the third month. A third sporadic type may arise late in fetal life, during the eighth or ninth month, which resembles the choroiditis in the adult and is heavily pigmented.

In our cases, if the inflammation had begun during the first three months of life there would have been a major abnormality or monstrosity of the eye. If the process had been severe before the fifth month the retinal vessels would not have been present, the retina would have been less differentiated and the sclera would have been thinned and bulging or cystic.

In case 1 the patient was an 8 month premature infant and the tissue was studied one month after birth (conception age, 9 months). The anterior and posterior segments showed largely the characteristic development of an eye of a 7 month fetus and partly the development of an 8 month fetus. The macular areas of the retina normally are late in differentiation (after the eighth month). The usual involvement of this part of the retina in infants may be related to the affinity of the parasite for young nerve

tissue. No adult ocular lesions have been reported in the acquired form of the disease.¹⁵

The process in our cases probably originated not later than the seventh month of gestation. The infection apparently retarded, and in some parts of the eye stopped, normal differentiation, as well as produced focal lesions.

While ophthalmoscopic examination may be difficult, owing to the small size of the eyes, the nystagmus and the poorly dilated pupils, the differential diagnosis of early lesions is otherwise relatively easy. The appearance of the bilateral retinal foci and related ocular signs and the general physical findings are usually convincing. The quiescent old lesions require differentiation from healed fetal and acquired chorioretinitis of various causes. Demonstration of neutralizing antibodies against the toxoplasma in the blood of a child and his parents, general physical and psychologic studies and examination of the spinal fluid aid in diagnosis. The extension of such studies to both normal persons and patients with suspicious chorioretinal scars may prove of value. The isolated healed lesions are not pathognomonic.

SUMMARY

Our cases gave opportunity for simultaneous study and description of pathologic lesions and lesions seen with the ophthalmoscope in identical twins. An attempt has been made to date the onset of the lesions on the basis of the developmental stages of the eye and the persistence of fetal structures. In both cases early ocular lesions were demonstrated and are thought to have originated in the seventh fetal month. Our cases demonstrate the destructive affinity of the toxoplasma for young nerve tissue, especially that of the eye.

The conceptional age, the virulence of the parasite and the special susceptibility of tissue may influence the distribution and the severity of the disease.

In the future, other parasites may be found to produce lesions similar to those of toxoplasmosis, hence the importance of a study of the parasite and its properties. The cases reported here offer strong evidence for transplacental infection.

¹⁵ Pinkerton, H., and Weinmann, D. Toxoplasma Infection in Mass., Arch Path 30:374-392 (July) 1940. Pinkerton, H., and Henderson, R. G. Adult Toxoplasmosis. A Previously Unrecognized Disease Entity Simulating the Typhus-Spotted Fever Group, J. A. M. A. 116:807-814 (March 1) 1941.

¹⁴ Mann, I. Developmental Abnormalities of the Eye. New York, Cambridge University Press, 1937, p 181.

FACTORS AFFECTING HEMORRHAGE FOLLOWING EXTRactions OF CATARACTS

E EUGENE NEFF, MD

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The problem of hemorrhage into the anterior chamber of the eye after the removal of a cataract has always been a disturbing one to ophthalmologists because the hemorrhage prolongs convalescence, it may lead to other complications and occasionally it results in limitation of vision. This problem has been baffling because it has been difficult to ascertain the cause of the hemorrhage.

Many papers dealing with various aspects of the problem have appeared, but three are outstanding among the earlier publications. Between 1869 and 1897 Herman Knapp¹ reported about 2,000 cases. He concluded that trauma accounts for the hemorrhage in a large number of cases but that in many others the cause is unknown.

In 1916 Wheeler² reviewed the literature thoroughly and also reported results for a total of 2,123 operations which had been done by various members of the staff of the New York Eye and Ear Infirmary during a ten year period while the type of operation was undergoing a transition from the technic of simple extraction to that of removal of the cataract either with or after iridectomy. He found that hemorrhage occurred least often after preliminary iridectomy and most frequently when the cataract was removed with simultaneous iridectomy. He also noted that a higher percentage of hemorrhages

Candidate's thesis for membership in the American Ophthalmological Society, submitted May 29, 1944

1 Knapp, H Report and Remarks on a Third Hundred of Cataract Extractions, Arch Ophth **1** 103, 1869, Report and Remarks on a Fourth and Fifth Hundred of Cataract Extractions According to von Graefe's Method, *ibid* **6** 3, 1877, Report and Remarks on a Sixth Hundred of Cataract Extractions Performed According to von Graefe's Method, *ibid* **8** 200, 1879, Report of a Seventh Hundred of Cataract Extractions with Historical and Critical Remarks, Particularly on the Peripheral Opening of the Capsule, *ibid* **10** 295, 1881, Report of an Eighth Series of One Hundred Consecutive Cataract Extractions with Remarks, *ibid* **12** 69, 1883, Report on a Second Series of One Hundred Successive Cataract Extractions Without Iridectomy, *ibid* **18** 1, 1889, Report of a Third Series of One Hundred Successive Cataract Extractions Without Iridectomy, *ibid* **19** 280, 1890, *Jahresb f Ophth*, 1897, p 95

2 Wheeler, J M A Study of Hemorrhage into the Anterior Chamber Subsequent to Operations for Hard Cataract, *Tr Am Ophth Soc* **14** 742, 1916

occurred in the 40 to 50 year old patients group and suggested that the greater activity of persons of this age group might be more significant in causing trauma than the dementia and irresponsibility of elderly patients.

Derrick Vail Jr published a careful study of the problem of hyphema in 1933³ and included the following points among his conclusions:

1 The incidence of hemorrhage, as derived from a review of the literature and as substantiated by his own work, was 76 per cent of the total number of operations for removal of cataracts.

2 Sex, age and general health play a minor role, if any, and the cause of hemorrhage is chiefly a local factor.

3 In the vast majority of cases hyphema is due directly to trauma.

4 A "constitutional moment" exists for the eye between the third and the sixth day, when external pressure is most likely to cause hemorrhage. This "constitutional moment" is related to the rapidity with which the anterior chamber fills, and hemorrhage apparently occurs more readily when a conjunctival flap and sutures give tight closure of the wound to hasten the filling process.

5 Hyphema occurred less frequently after simple extraction, with which filling of the anterior chamber was less rapid, but prolapse of the iris was a common and serious complication with this operation.

6 Preventive treatment is important, the time of the first dressing being critical and careful nursing for the first seven days essential.

From these studies it is apparent that trauma is an important cause of hemorrhage. The type of operation and its effect on intraocular pressure are responsible for the hyphema in some cases. Certain unknown factors likewise play a role. In an effort to understand these factors I began an investigation in which each patient was carefully studied. That I might be able better to evaluate the factors which cause hemorrhage, I undertook detailed examinations of the

3 Vail, D T, Jr On Hyphema After Cataract Extraction, *Tr Am Ophth Soc* **31** 496, 1933

blood and the physical status of the patient. While my study was in progress, a few additional reports which are of interest appeared in the literature.

In 1941 Vail reported⁴ an additional series of 675 cases to substantiate his theory that trauma is important but that increased intraocular pressure from rapid filling of the anterior chamber predisposes to hemorrhage.

In 1942 Gradle and Sugar⁵ published results of an interesting study in which they had attempted to evaluate the forces which might affect the degree of tension in a cataract wound. They measured the increase in intraocular pressure due to the forcible contraction of the orbicularis palpebrarum, the compressibility of the orbital tissues and the degree of protrusion of the eyeball. They concluded that the first of these factors is the most significant, and accordingly they performed a series of 40 operations on private patients using tenotomy of the orbicularis muscle to lessen the chance of increasing intraocular pressure. Their results were 100 per cent successful, and no rupture of the wound or hemorrhage occurred in any patient. In a second series of 52 infirmary patients, however, 9 hemorrhages were noted. This work would appear to substantiate both Vail's theory that external pressure can cause hemorrhage if applied at a critical time and Knapp's and Wheeler's suggestion that unknown factors are significant.

In 1942 DeVoe⁶ presented a summary of 453 operations for cataract. He had studied various factors which might have caused hyphemia, and in his report he compared the average values for patients who had had postoperative hemorrhage with those for patients who had not bled. His total incidence of hemorrhage was 20.9 per cent. He stated that age, time of year, systolic and diastolic blood pressure, the presence of diabetes or syphilis and elevated intraocular pressure were not found to be related to postoperative hemorrhage. Also the type of operation, the presence or absence of retrobulbar injection, the type of suturing and the skill of the surgeon were not significant, although the performance of an iridectomy at the time of extraction increased the chance of subsequent hemorrhage by about 20 per cent. DeVoe's determinations of the level of ascorbic acid in the plasma and his tests for capillary fragility gave values which lacked cor-

relation and which were not reliable in predetermining hemorrhage. He concluded that neither vitamin C subnutrition nor a deficiency of prothrombin in the plasma associated with lack of vitamin K is an important cause of hemorrhage following extraction of cataract. Certain systemic measures, such as the use of snake venom, calcium, thromboplastic substances, protein diets and various proprietary drugs, were tried but did not appear useful as preventive agents of hyphemia.

Although DeVoe has made a careful, critical summary of a large number of cases, his gross analysis has failed to reveal the factors which are routinely responsible for hemorrhage. I have approached the problem from a slightly different point of view. Instead of utilizing only average results or statistical analyses, I have attempted to evaluate individual cases. For this purpose I have done complete blood counts and platelet counts, measured the bleeding time and the coagulation time, made clot retraction and tourniquet tests, taken the blood pressure and made determinations of hemoglobin, blood sugar and nonprotein nitrogen, as well as made a complete physical examination of each patient, together with a review of his past tendencies toward bleeding.

A few authors have mentioned similar but less complete studies of the blood, but none has reported results for a carefully controlled series of cases. Turner⁷ stated in 1935 "The coagulation and bleeding time should be taken. If these do not conform to good surgical practice, the operation should be postponed until this element can be corrected or the risk minimized." Goar⁸ in 1938 advised preliminary administration of calcium if the bleeding or the clotting time is long. Berens and Bogart⁹ (1938, 1941) did determinations of coagulation and bleeding time in addition to the usual blood counts and hemoglobin estimations, but these authors have not presented the details of their results. They considered increased intraocular tension an important predisposing factor for hyphemia. Meyer¹⁰ in 1929 measured the platelets, the serum calcium, the bleeding time, the coagulation time, the capillary fragility and the excretion of vitamin C of 8 patients; he found a correlation between deficiency of vita-

7 Turner, H. H. Preoperative Study of Cataract Patient, Pennsylvania M J 38:840, 1935

8 Goar, E. L. Management of Complications of Intraocular Surgery, Am J Surg 42:62, 1938

9 Berens, C., and Bogart, D. Postoperative Complications of Cataract Extraction, Am J Surg 42:39, 1938, Immediate Complications of Operations for Acquired Cataract, ibid 54:346, 1941

10 Meyer, F. W. Ueber die postoperative Nachblutung nach Starextraktion und ihre Ursachen, Klin Monatsbl f Augenheil 102:479, 1929

4 Vail, D. T., Jr. Hyphema After Cataract Extraction, Am J Ophth 24:920, 1941

5 Gradle, H. S., and Sugar, H. S. Wound Rupture After Cataract Extraction, Am J Ophth 25:426, 1942

6 DeVoe, G. Hemorrhage After Cataract Extraction. A Clinical and Experimental Investigation of Its Cause and Treatment, Arch Ophth 28:1069 (Dec) 1942

min C and of capillary fragility in 7 of them Taube¹¹ in 1938 had bleeding at an operation for preliminary iridectomy in a case in which the tourniquet test gave a positive reaction for capillary fragility. The cataract was removed successfully after vitamin C therapy had been given for four weeks. Urbanek and Albrecht¹² (1938) found the incidence of hemorrhage higher in an institutional group whose deficit in vitamin C (measured by tests of excretion) was greater than was found for private patients. Foss¹³ (1941) determined the prothrombin time for 54 patients with cataract and concluded that hemorrhage is not due to a deficiency of vitamin K. The reports of these authors give some clues in regard to constitutional conditions which may cause bleeding after operations for cataract. The purpose of my investigation has been to study these factors in more detail so that they may be evaluated in relation to the whole problem of hyphemia.

METHODS

The following techniques have been employed in my study of individual patients. Whenever possible, determinations were done in duplicate to insure accuracy of results. Many of the tests were done in the special hematologic laboratory¹⁴

1 Red and white blood cells were counted and hemoglobin determinations made on fasting oxalated whole venous blood. The blood was diluted with Hayem's solution for the red cell counts and with 1 per cent acetic acid for the white cell counts. A Neubauer counting chamber was used. Hemoglobin was determined by means of photoelectric colorimetry. In preparing slides for differential counts of leukocytes Wright's stain was used, and 100 cells were counted.

2 The number of blood platelets was determined by direct counts on capillary blood with the aid of an isotonic diluting fluid containing a stain and an anticoagulant, according to the method of Pohle (1939).¹⁵

3 Bleeding times were determined from a puncture of the lobe of the ear by the method of Duke, the blood being blotted every fifteen seconds on absorbent paper to estimate the rate of decrease and the final cessation of hemorrhage. The normal for this technic has been reported to be from one to three minutes.

4 Coagulation times were measured on venous blood by the method of Lee and White as modified by Pohle.

11 Taube, E L. Cataract Extraction in Subclinical Scurvy, Am J Ophth **21** 910, 1938

12 Urbanek, J., and Albrecht, W. C-Vitamin und Lebensalter, Ztschr f Augenhe **95** 129, 1938

13 Foss, B. Gibt es eine K-Vitamininsuffizienz bei Blutungen nach intrabulbären Eingriffen? Acta ophth **19** 15, 1941

14 Dr O O Meyer has made suggestions and has supervised the hematologic studies for this investigation. Dr F J Pohle has personally performed many of the determinations.

15 Pohle, F J. The Blood Platelet Count in Relation to the Menstrual Cycle in Normal Women, Am J M Sc **197** 40, 1939

and Taylor¹⁶ (1937). Two small test tubes were filled with 2 cc each of venous blood and kept at 37°C. From time to time the first tube was gently tilted to test for the onset of clotting. The second tube was kept in reserve and tested as coagulation started in the first tube, thus serving as a check on accuracy. Normal values were between six and twelve minutes.

5 Clot retraction times were measured by observing the number of hours before 2 to 3 cc of clotted blood began to separate from the wall of the test tube with beginning expression of serum.

6 The Rumpel-Leede tourniquet test was used to determine capillary fragility. A pressure midway between systolic and diastolic was maintained for seven and one-half minutes by means of a blood pressure cuff applied just above the elbow. Petechiae were counted in a 1 inch (2.5 cm) square 2 inches (5 cm) below the antecubital fossa after the cyanosis had cleared. From 0 to 12 petechiae were considered normal, 12 to 20 were considered an equivocal value, and more than 20 were thought to afford positive indication of capillary fragility.

7 The sugar content and the nonprotein nitrogen content were determined on fasting, oxalated, whole venous blood by the classic Folin and Wu copper reduction method for sugar and a micromodification of the Kjeldahl-Folin technic for nonprotein nitrogen.

The following standards were used in estimating hyphemia:

1 A small amount of blood found in the anterior chamber at the time of the first dressing was considered hemorrhage from the surgical operation.

2 Any amount of blood appearing after the first dressing was considered postoperative bleeding.

3 Degrees of hyphemia were based on the following criteria: 1 degree, 1 mm or less of blood in the anterior chamber, 2 degrees, $\frac{1}{4}$ mm of blood in the anterior chamber, 3 degrees, the anterior chamber full of blood, 4 degrees, the anterior chamber full of blood plus opening of the wound.

RESULTS

In the series which I am reporting there were only 98 patients, but an attempt has been made to make a thorough study of each. Before I discuss the details and the significance of my results, it is interesting to note the conclusion which is reached if averages are studied. My patients with cataract have been divided into two groups according to whether or not they had postoperative hemorrhage. Table 1 presents a summary of the range and the average results of the tests which were used to evaluate the status of each patient. I wish to call attention to the fact that the average values for patients with hemorrhage are not significantly different from the average results for patients who did not have postoperative bleeding. Thus, at first glance my work would seem to confirm the conclusions of those previous authors who have stated that age, systolic and diastolic blood pressure, anemia,

16 Pohle, F J., and Taylor, F H L. The Coagulation Defect in Hemophilia. The Effect in Hemophilia of Intramuscular Administration of a Globulin Substance Derived from Normal Human Plasma, J Clin Investigation **16** 741, 1937.

platelet level, bleeding time, coagulation time, results of tourniquet tests and the existence of diabetes or nephritis are not significant factors for predicting the occurrence of postoperative hemorrhage.

A total of 205 operations were performed on the 98 patients.¹⁷ They have been summarized in table 2 according to the type of operation and the number of hemorrhages. In chart A the data are graphically presented, with the results grouped together for each ten year age period. The operations which were followed by hemorrhage have been divided according to whether or not known trauma was responsible for the bleeding.

It is at once apparent that the greatest frequency of hemorrhage took place with the combined intracapsular extractions. In this group of operations the incidence of bleeding was 20.6 per cent, in contrast to 7.8 per cent for intracapsular extractions after preliminary iridectomy.

theories of Wheeler and Vail that the type of operation and trauma are two important factors influencing postoperative bleeding.

Since the results thus far summarized do not contribute any new insight into the problem of hyphemia and since the use of averages obscures factors which may be important, I have prepared table 3 to present some pertinent facts about the individual patients of my series. In this table are included the more important laboratory data for all patients who had postoperative hemorrhage. When the data for patients without known trauma are contrasted with the data for patients whose bleeding was precipitated by trauma, the following findings appear worthy of comment:

1 As has been previously noted, the greatest number of hemorrhages occurred with combined intracapsular extractions. Trauma had no special significance in these cases, since 6 of the 13 patients had had no known trauma.

TABLE 1.—Data on Patients Having Cataract Operations

No. of patients without hemorrhage	Age	Blood Pressure		Non-protein Nitrogen	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Bleeding Time	Coagulation Time	Tourniquet Test	
		Systolic	Diastolic									
77	Age	230	130	132	45	17.6	7.15	15,800	394,000	4	12.5	28*
High	50	230	130	132	45	17.6	7.15	15,800	394,000	4	12.5	28*
Low	34	96	50	55	24	11.1	3.6	5,000	145,000	1	3.5	0
Average	65	152.7	87.4	114.9	35.4	14.3	4.6	9,500	273,800	1.6	7.1	2.9
21 patients with postoperative bleeding												
High	83	198	115	110	42	17.6	9.25	12,250	320,000	3	9	18
Low	59	106	70	72	20	6.6	3.93	5,000	175,000	1	3	0
Average	67	145.7	92.1	95.7	33.3	15.2	5.3	8,900	261,600	1.4	6.5	4.6

* Two patients with values of 68 and 49, which were corrected after vitamin C therapy to 17 and 2, were not included in this table.

TABLE 2.—Summary of Types of Operations and the Number of Hemorrhages for Each

Type of Operation	No. of Operations	No. of Patients	No. of Hemorrhages
Preliminary iridectomy	62	43*	2
Intracapsular extraction after preliminary iridectomy	51	36	4
Extracapsular extraction after preliminary iridectomy	11	7	0
Combined intracapsular extraction	63	29	13
Combined extracapsular extraction	18	16	4
Total	205	98	23

* These are not included in the total.

tomies. There were only 3.2 per cent of hemorrhages following preliminary iridectomies. The total incidence of hyphemia for the whole series was 11.2 per cent. Trauma was known to be instrumental in 48 per cent of the cases of hemorrhage. These results substantiate the

17 These operations were executed by both attending doctors and resident staff members at the Wisconsin General Hospital. The technic for the intracapsular extractions and the preoperative and postoperative care of the patients has been discussed in detail by Davis (*Personal Experiences with Intracapsular Cataract Extractions*, *Trans Am Acad Ophth* 42:235, 1937).

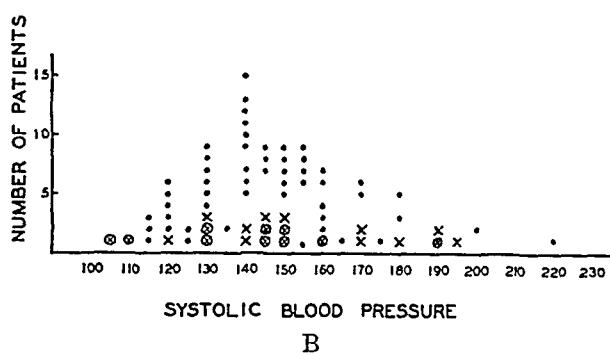
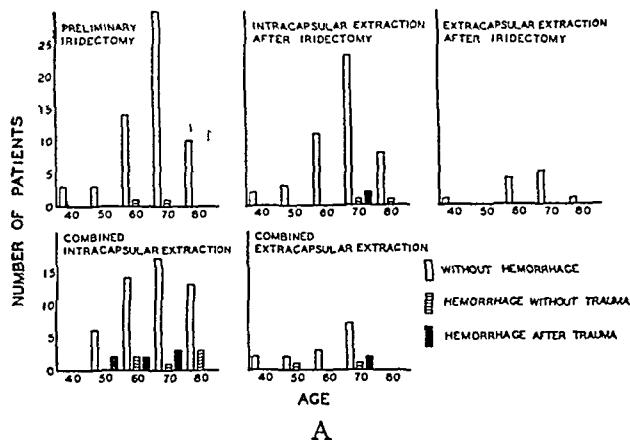
2 The severity of the hemorrhages was comparable for the patients who had undergone trauma and for those who bled without known trauma. Among patients without trauma there were 6 instances of 1 degree hyphemia and 3 instances each of 2 degree and of 3 degree hyphemia. In the traumatic group 4 patients had 1 degree, 5 had 2 degrees and 2 had 3 degrees of hyphemia. There was no occurrence of 4 degree hyphemia.

3 Hemorrhages occurred from the third to the twelfth day after preliminary iridectomy. They occurred more often at about five or six days for the series as a whole. This result is in accord with the experience of other workers.

4 The occurrences of hemorrhage were equally divided between men and women for those who bled without trauma, but 80 per cent of those who bled after trauma were men. Perhaps males are more prone to have traumatic episodes.

5 Blood pressures for my entire series ranged from 96 systolic and 50 diastolic to 230 systolic and 120 diastolic, varying in the bleeding patients from 106 systolic and 74 diastolic to 198 systolic

and 108 diastolic. The hemorrhages were about equally distributed throughout the entire range of these blood pressures, but 5 patients without trauma had a systolic pressure higher than 150 with a diastolic pressure of over 100, in contrast to only 1 hypertensive patient among those with trauma. The latter bled after each of two operations. In chart *B* the systolic pressures are

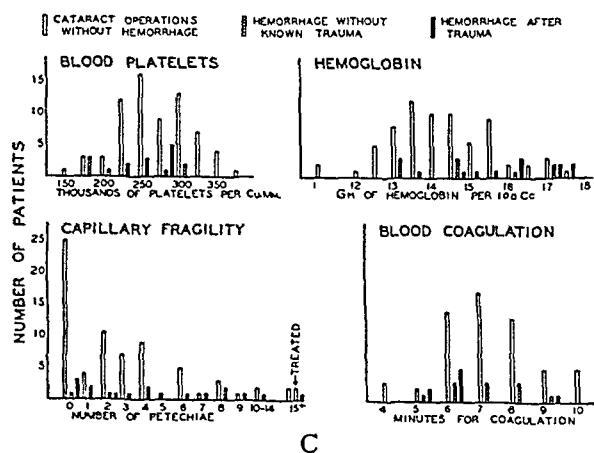


without the added tension produced from trauma. Diastolic pressures have not been charted, but they closely followed the systolic pressures in deviations from the normal.

6 Only 3 patients among those with hemorrhage were markedly overweight or underweight, and all of these were in the group whose bleeding took place after trauma. This may or may not mean that malnutrition when manifest as underweight or as overweight is important in relation to hyphemia. Undoubtedly malnutrition might be significant if it were correlated with those deficiencies in minerals or in vitamins which have a direct relationship to hemorrhagic tendencies.

7 Four patients among those with hyphemia had blood platelet levels of about 200,000 or lower. It seemed pertinent, therefore, to study all patients graphically with respect to platelet levels, and the results are shown in chart *C*. It will be noted that the incidence of hemorrhage was much greater for the lower platelet levels and that nearly one half of all patients with blood platelet levels below 200,000 had postoperative bleeding. Trauma was not required to initiate the bleeding of any patient who had a platelet level below 250,000. Thus the platelet level may be one of the factors which are important for determining whether or not bleeding will take place after an operation for cataract, and trauma is less significant as a factor in causing hemorrhage for patients who have low blood platelet counts.

8 There was more tendency toward bleeding among patients with high levels of hemoglobin than among patients with average levels of hemoglobin in their blood. Chart *C* shows that 6 of the 10 patients with values of 17 to 18 Gm of hemoglobin had hyphemia and that 4 of the 8 patients with 16 to 17 Gm of hemoglobin also bled. It also shows that trauma was an additional factor in 2 of the 6 hemorrhages reported at the 17 Gm hemoglobin level and for 3 of the 4 shown at the 16 Gm level. Thus it is not known whether the trauma or the high level of hemoglobin had the greater significance in producing the bleeding. Hypertension was an additional factor in 2 patients, and 2 others had low blood platelet values, a fact which indicates that factors other than the hemoglobin level may have been decisive in causing the bleeding. One of the patients who bled repeatedly and severely without trauma, however, was diagnosed as having polycythemia vera. Venesection before a subsequent operation was successful in preventing further hemorrhages in this patient. Only 1 patient was seriously anemic, with a hemo-



A, distribution of 205 operations for cataract on the basis of type of operation, age and incidence of hemorrhage. *B*, the relation of blood pressure to hemorrhage. Dots represent operations for cataract not followed by hemorrhage; crosses represent postoperative hemorrhage without known trauma; encircled crosses represent hemorrhage following trauma postoperatively. *C*, factors affecting postoperative hemorrhage.

illustrated for all 98 patients. This graphic presentation helps one to visualize the fact that hypertensive patients are more likely to bleed

globin content of 6.6 Gm. This patient bled after trauma.

9 The data for the tourniquet test of capillary fragility are presented in both table 3 and chart C. In the group who had 2 or fewer petechiae in their tests there were 40 patients who did not bleed, in contrast to the 8 who did have hemorrhage. Six of the latter had trauma.

had the exceptionally high petechial counts of 68 and 49 were given vitamin C therapy before surgical procedure was begun. Operations were successfully performed without the occurrence of hemorrhage after their petechial counts had been reduced to 17 and 2 respectively.

10 The coagulation time did not appear to be an important factor in hyphemia, but less

TABLE 3.—Data on the 21 Patients Having Postoperative Hemorrhages

Sequence and Type of Operation*	HypHEMA		Age	Sex	Blood Pressure	Hemo globin, Gm	Platelets	Bleeding Time, Min	Coagu lation Time, Min	Tour niquet Test, Petechiae	Cause of Trauma
	Degree	Day									
CEE	1	5	50	M	150/94	14.9	284,000	2	7	8	
PI	—	6	71	M	144/104	17.0	186,000	1	8	4	Out of bed
OIE	1	6	71	M	144/104	17.0	186,000	1	8	4	Out of bed
IAP	2	6	71	M	144/104	17.0	186,000	1	8	4	Out of bed
CIE	3	6	75	M	120/70	14.7	175,000	1	5	5	
CIE	1	7	75	M	130/80	14.9	312,000	1.5	6	0	
CIE	1	5	76	M	172/108	17.1	300,000	1	6	7	
CIE	—	—	76	M	172/108	17.6	300,000	1	6	7	
PI	—	11	83	M	198/108	13.0	247,000	1	6	6	
IAP	1	4	55	F	125/75	17.6	249,000	1	7	8	
CIE	2	4	55	F	125/75	17.6	249,000	1	7	8	
PI	—	—	—	—	—	—	—	—	—	—	—
EAP	—	—	—	—	—	—	—	—	—	—	—
OIE	2	9	58	F	170/110	15.1	306,000	3	8	4	
PI	—	—	—	—	—	—	—	—	—	—	—
IAP	1	3	59	F	180/108	17.6	204,000	3	7	3	
CEE	—	—	—	—	—	—	—	—	—	—	—
CEE	1	4	70	F	190/115	16.1	184,000	2.5	9	18	
PI	—	—	—	—	—	—	—	—	—	—	—
EAP	—	—	—	—	—	—	—	—	—	—	—
PI	—	—	—	—	—	—	—	—	—	—	—
EAP	—	—	—	—	—	—	—	—	—	—	—
OIE	1	5	51	M	190/110	16.1	281,000	1	6	0	Bumped eye
CIE	2	5	51	M	162/108	16.1	281,000	1	6	0	Sneezed
CIE	2	5	59	M	106/74	6.6	279,000	1	6	1	Removed dressing
CIE	1	6	61	M	110/80	16.4	280,000	1.5	6	2	Struck eye
CIE	2	6	65	M	130/70	16.4	250,000	1	9	9	Rolled on to eye
PI	—	—	—	—	—	—	—	—	—	—	—
PI	—	—	—	—	—	—	—	—	—	—	—
IAP	2	5	72	M	134/90	13.6	275,000	1	5	0	Bumped eye
IAP	—	—	—	—	—	—	—	—	—	—	Removed dressing
CIE	1	4	72	M	150/110	17.1	283,000	1	6	0	Bumped eye, out of bed
CEE	3	6	73	M	146/90	15.8	274,000	1.5	5	1	Struck eye
CEE	1	4	73	M	160/88	17.1	320,000	1	3		Plucked at bandage
CIE	2	5	66	F	152/88	14.9					Startled, sat up
PI	—	—	—	—	—	—	—	—	—	—	—
IAP	3	5	72	F	145/85	13.4	260,000	1.3	6	10	Disoriented
PI	—	—	—	—	—	—	—	—	—	—	Removed dressing

* Key to abbreviations in this column: PI, preliminary iridectomy; IAP, intracapsular extraction after preliminary iridectomy; EAP, extracapsular extraction after preliminary iridectomy; CIE, combined intracapsular extraction; OEE, combined extracapsular extraction.

as a factor in producing the hemorrhage. The incidence of hemorrhage was much higher among the patients with higher petechial counts. Of the 15 patients with petechial counts of 7 or higher, 6 had postoperative bleeding, but in only 2 of these was trauma an additional factor. Thus, hemorrhage is more common and trauma less significant when the tourniquet test indicates greater capillary fragility. Two patients who

trauma was required for bleeding among patients with higher coagulation times.

11 No abnormal values for clot retraction were found for any of the patients of my series, and the bleeding times for all were within the range of one to three minutes.

12 Past histories of the patients in regard to tendencies toward bleeding were unreliable for predicting whether or not hemorrhage would

occur with the extraction of a cataract. Ten of the patients gave past histories of easy bleeding or bruising, but only 2 of these had hyphema at the time of operation. These 2, however, bled without known trauma.

13 Since trauma was a factor in one half of the cases of hemorrhage, I have included in table 3 the types of accidents that occurred. Five patients bumped or struck their eyes, 1 rolled onto his eye, 4 plucked at or removed their bandages, 2 got out of bed, 1 sneezed violently and 1 was startled and sat up suddenly when a window blew open. It is evident that only the last 2 of these happenings were unavoidable accidents. It is well known that the management of these patients is difficult, but it would seem that if more care were taken in advance to gain their cooperation at least some of these accidents might be avoided.

COMMENT

My data apparently confirm the work of others who have found a higher incidence of hemorrhage after combined intracapsular extractions. I should like to suggest, therefore, that preliminary iridectomies should be done whenever possible. In a state hospital this is frequently impossible, but it is worth considering when time and expense need not be so closely considered.

The details of these data have been presented in the hope that they may be of service in bringing the problem of postoperative hemorrhage closer to solution. I am well aware that this evidence cannot be considered a final answer. It seems, however, that this critical analysis of individual cases brings out significant findings which are concealed or obscured when only average results in a large series are considered. It also seems

that the separate analysis of cases with and without known trauma has brought greater insight into the factors which cause bleeding. These data tend to emphasize the importance of the physical status of the patient. In those patients whose bleeding was initiated by trauma the results of the tests were within a more normal range. In those patients who bled without traumatic incidents abnormal values (or values at the upper and lower ranges of what has been considered normal) were commonly found. Most significant among such abnormal values were hypertensive levels of systolic and diastolic blood pressures, low blood platelet values, both low and high amounts of hemoglobin, capillary fragility as indicated by positive results of tourniquet tests, and increased blood coagulation times. I assume that none of these factors is of absolute importance in causing the bleeding but that the actual hemorrhage occurs when the proper combination of circumstances is present.

SUMMARY

The type of operation and the application of trauma at a critical time are two fundamentally important factors in causing bleeding after surgical intervention for cataract, but the constitutional background of the patient has a definite significance. The tests mentioned in this report cannot be used to predict which patient will have postoperative hemorrhage, but they can point out abnormalities that make bleeding more likely. Whenever possible, grossly abnormal conditions should be corrected before any operation is performed. I should like to reiterate Vail's suggestion as to the importance of preventive treatment and his emphasis on the critical time during the first seven days and on the need for careful nursing.

GLAUCOMA DUE TO PERIPHERAL ANTERIOR SYNECHIAS AFTER OPERATION FOR CATARACT

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CHICAGO

The multiple factors which influence the intraocular pressure are so closely interrelated and regulated in the normal human being that it is almost impossible to attribute a given rise in intraocular pressure to the action of any single factor. Even in the case of the best known rise occurring in the normal human eye, that during Valsalva's experiment, one is unable to decide whether the cause is an increased volume of blood in the uvea or an interference with the function of Schlemm's canal. Ocular disease occasionally singles out one of the main factors concerned with the regulation of the intraocular pressure and thus creates a glaucomatous state with a much simpler mechanism than that underlying the normal intraocular pressure. A classic example of such a glaucomatous state is the one caused by peripheral anterior synechias following prolonged absence of the anterior chamber after operation for cataract. It is reasonably certain that in eyes affected in this way normal conditions prevailed before the operation with regard to the balance of the intraocular pressure and that only the outflow of intraocular fluid became disturbed by the formation of peripheral anterior synechias. The detailed study of such eyes promised to yield information of value for the understanding not only of this type of glaucoma but also of problems of regulation of the intraocular pressure in general. It was for these two reasons that the present study was undertaken.

MATERIAL

This study concerns itself with states of persistently elevated intraocular pressure of aphakic eyes in which (1) careful examination before the extraction of the cataract, including at least one tonometric reading, had revealed no sign of glaucoma, (2) the inflammatory postoperative reaction was slight and either had completely subsided or was definitely diminishing in intensity fourteen days after the operation, (3) the anterior chamber had been absent for at

least six days after the operation, (4) extensive peripheral synechias were found on gonioscopic examination, (5) the severity of the glaucoma closely paralleled the extent of the peripheral anterior synechias, and (6) observation of the normal mate after the surgical procedure revealed no sign of glaucoma.

All services of the Illinois Eye and Ear Infirmary were combed for cases that met the foregoing requirements. Invariably in the cases found no sutures or only conjunctival sutures had been used during the operation for cataract. Thus it appears highly probable that the absence of the chamber was caused by external fistulation. In several cases it was shown that the synechias preceded the glaucoma and did not change in extent during the continuance of the latter except as the result of operations.

The following phenomena were made the subject of study: (1) the diurnal variations of the intraocular pressure, (2) the response to parasympatholytic mydriatics, (3) the response to the drinking test, (4) the response to the puncture of the anterior chamber, (5) the response to corneal massage with the tonometer of Schiøtz for two minutes with the 15 Gm weight, (6) the response to pilocarpine.

After admission and acclimation to the hospital most patients showed diurnal variations of a regular pattern. The taking of measurements was restricted to intervals of four hours to reduce the possibility of thereby altering the intraocular pressure. The curve was invariably of the inverted type, with the low value at 2 a.m. and the high point between 10 a.m. and 2 p.m. (chart 1). At 2 a.m. the patients had to be wakened for the tonometric measurement, at 6 a.m. they were all awake, their morning activities having started only a few minutes before. The slope of the rise was greater than that of the fall. In corroboration of previous findings of Raeder¹ and Kronfeld,² the morning rise could be prevented by keeping the patients asleep or could be precipitated earlier by mild exercise at 2 a.m. (chart 2A).

Read at the Eightieth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 29, 1944. Dr Haas cooperated in the preparation of this paper by invitation.

¹ Raeder, J. G. *Klin Monatsbl f Augenh* **74**: 424, 1925.

² Kronfeld, P. C. *Am J Ophth* **16**: 881, 1933.

In 1 case with extreme daily fluctuations the depth of the anterior chamber was measured at the time of the high and of the low pressure by two independent observers. In or near the visual axis the apparent depth of the chamber was slightly but definitely greater at the time of the high pressure (2.47 against 2.12 mm.)

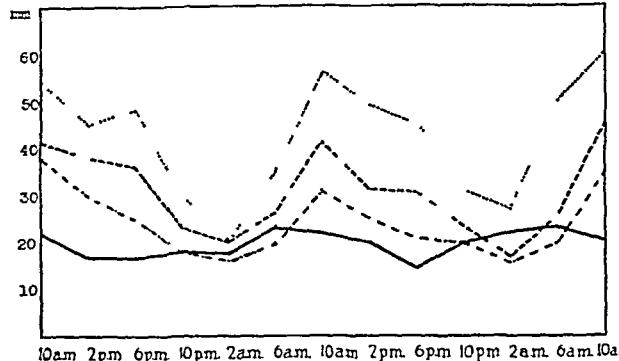


Chart 1—Characteristic diurnal variations. Solid line represents measurements for normal subject, dots and dashes, those for patient 1, dashes, those for patient 2, dotted line, those for patient 3.

relatively high and could be raised but slightly by glycerin

Of the parasympatholytic mydriatics, homatropine hydrobromide in 2 per cent concentration was used in the form of instillations at three consecutive tonometric examinations. When given at 10 a.m., 2 p.m. and 6 p.m. it had a definite pressor, or drop-retarding, effect (chart 2B). When it was given at 6 p.m., 10 p.m. and 2 a.m., that is, toward the end of the decline of the intraocular pressure there was hardly any immediate or late effect. The gonioscopic appearance of the peripheral anterior synechias was not appreciably altered by the instillation of the homatropine hydrobromide.

The drinking tests were done in the morning toward the end of the upgrade or in the early afternoon at the beginning of the downgrade. The result was strikingly positive in all cases a sharp rise being superimposed on the rising or the falling curve (table 1 and chart 3A)

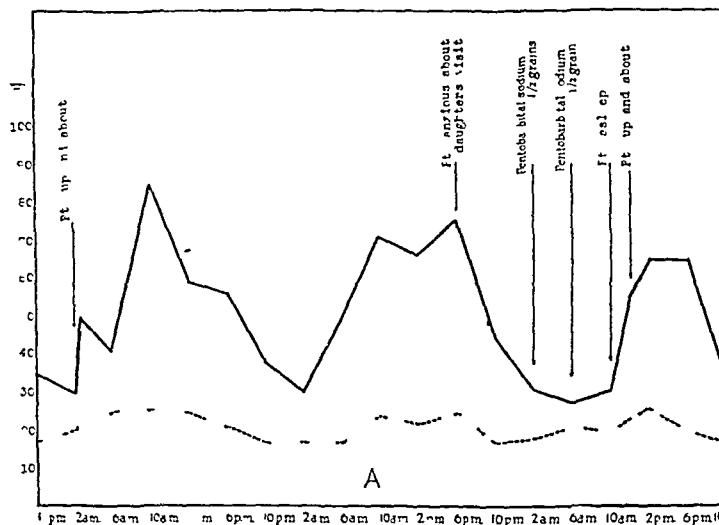
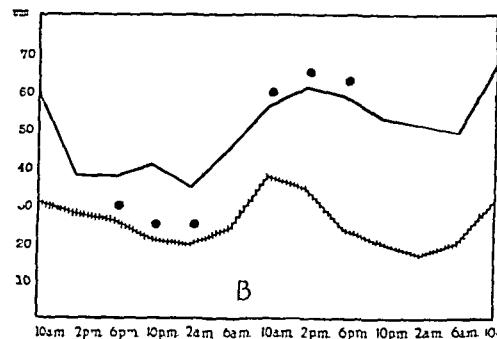


Chart 2—A, relation between sleep and intraocular pressure (patient 3). Solid line represents measurements for glaucomatous eye, dashes, for normal eye. B, response to homatropine bromide. Crosses represent measurements for patient 1, solid line, those for patient 5, dots, those after administration of 1 drop of homatropine bromide.



In several cases determination of the ocular rigidity after the method of J. Friedenwald³ was attempted at the time of the turning points. While we are convinced that the Schiøtz tonometer of today is not an adequate or satisfactory instrument for determining rigidity, there was consistency in our findings. The ocular rigidity of patients with small excursions was found not to vary with the intraocular pressure. The rigidity of the patient with extreme fluctuations previously mentioned was lower during the high phase but could repeatedly be raised by instillation of glycerin, which caused disappearance of all visible corneal edema. During the low phase without visible corneal edema the rigidity was

TABLE 1—Drinking Test

	Controls	Glaucomas					
		1	2	3	4	5	6
Intraocular pressure before	Average 20	26	45	65	35	26	35
Intraocular pressure after *	Average 25	40	60	110	56	49	50

* Highest reading obtained during the 60 minutes following ingestion of 1000 cc of water.

The response to the puncture of the anterior chamber was a characteristic one in eyes with mild or moderate elevation of the intraocular pressure. The initial drop reached immeasurably low values. The restoration time, that is, the interval necessary for the intraocular pressure to return to the original level, was about as long as or slightly longer than in nonglauco-

matous eyes with chambers having the same volume. The hypertensive phase was absent or slight, both absolutely and as compared with hypertensive phases observed in wide angle glaucomas of the same initial intraocular pressure. The hypotensive phase was also slight or unnoticeable. During the two hours after the puncture of the anterior chamber the non-glaucomatous mate showed a corresponding slight rise of the intraocular pressure.

In 1 patient with marked elevation of the intraocular pressure, two punctures of the anterior chamber were made, at an interval of thirteen days. At the time of the first puncture (7 p.m.) the initial pressure was 53 and was restored in ninety minutes. At the time of the second puncture (7 a.m.) the initial pressure was 53 and was restored in sixty minutes. The same amount of fluid, namely, 0.25 cc., was withdrawn at each puncture. The restoration of pressure in absolute terms was faster in the morning than in the afternoon (table 2).

they would probably show a greater drop during the massage test than nonglaucomatous eyes with initial pressures of from 25 to 33. In the light of this consideration the drop observed in our cases of glaucoma appears very small (table 3). This would tend to substantiate the

TABLE 3—Massage Test

	Controls	Glaucomas									
		1	2	3	4	5	6	7	8	9	
Intraocular pressure before massage	32-39		32	33	65	38	15	32	32	28	52
Intraocular pressure after massage	Average 18 (drop never less than 10)	28	32	61	32	39	28	24	22	15	

belief that the massage test is partially indicative of whether the trabeculae and the canal of Schlemm are functioning normally.⁵

Pilocarpine nitrate was effective during the ascent as well as during the descent. It inhibited

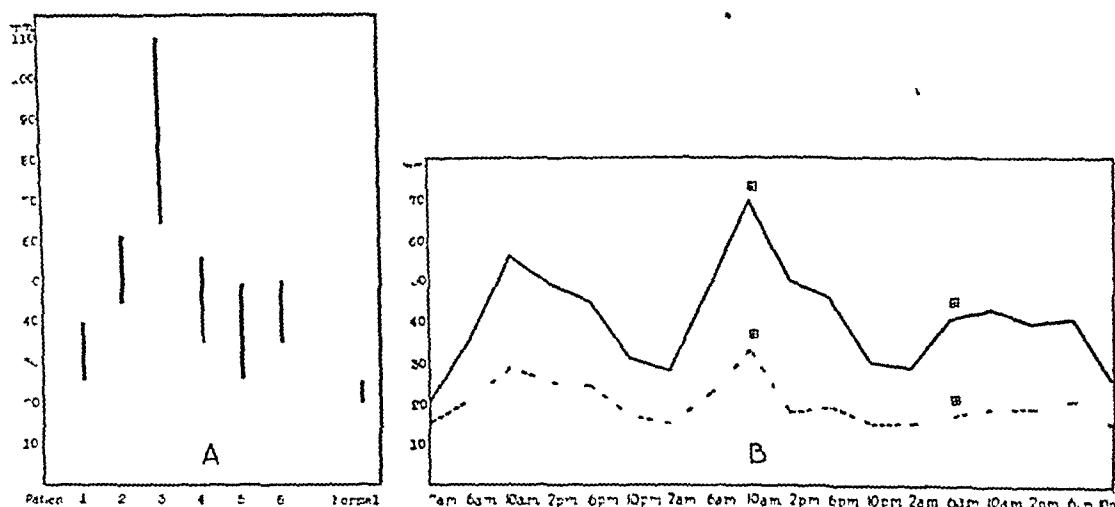


Chart 3—A, results of drinking test. B, response to a 2 per cent solution of pilocarpine nitrate. Solid line represents measurements for patient 3, dashes, those for patient 6, crosses in squares, those after administration of 1 drop of pilocarpine nitrate.

TABLE 2—Restoration of Intraocular Pressure After Puncture of the Anterior Chamber

Time	7 00	7 30	8 00	8 30
P.M.	53 (ACP)	4	38	53
A.M.	53 (ACP)	23	33	

The immediate drop in intraocular pressure due to corneal massage was characteristically slight in all cases. For normal, nonglaucomatous eyes Boeck, Kronfeld and Stough⁴ had shown a dependence of the drop on the initial level of pressure, the drop being greater in eyes with higher initial pressure. If nonglaucomatous eyes existed with initial pressure of from 32 to 40

the former and made the latter more precipitous. A single dose of 2 per cent pilocarpine nitrate solution given at 6 a.m. in all cases of mild elevation of pressure prevented a further rise almost completely (chart 3 B). Without further medication the next rise in pressure took place the following morning.

COMMENT

The data reported in the foregoing section have a bearing on the diagnosis and the treatment of this form of glaucoma. Tonometric measurements made at or around noon are most likely to reveal the highest pressure reached by the individual patient. Of the provocative tests, introduction of a mydriatic and puncture of the

⁴ Boeck, J., Kronfeld, P. C., and Stough, J. T. Effect on Intra-Ocular Tension of Corneal Massage with Tonometer of Schiotz, Arch Ophth 11: 797 (May) 1934.

⁵ Kukan, F. Klin Monatsbl f Augenh 100: 68, 1938.

anterior chamber are not likely to give definitely abnormal results. The massage test and especially the drinking test are more likely to reveal an insufficiency of the apparatus regulating the intraocular pressure.

With regard to conservative therapy, it would seem reasonable to use the miotics during the early morning to prevent the usual morning ascent of intraocular pressure. The first application should be made "the very first thing in the morning," and this should be followed by one to three additional applications during the course of the morning if necessary. During the afternoon and during the night these eyes more or less take care of themselves. An application before the patient retires would be wasted, since its effect would not last until the next morning.

With regard to the possible mechanism of these glaucomas, we are well aware of the dangers of overly simplified concepts. In a system with impaired though probably still adjustable outflow a rapid rise in intraocular pressure from normal or high normal to definitely pathologic levels of pressure might be due to (1) extraocular conditions like lack of the massage action of the extrinsic muscles and the orbicularis, (2) an increase in the volume of blood in the uvea at a rate exceeding the capacity of the

channels of outflow, (3) the production of intraocular fluid at a rate exceeding the capacity of the channels of outflow.

Factor 1 could not account for the elevation of the intraocular pressure, since the latter corresponded to periods of increased activity on the part of the patient. Several of our observations would seem to make factor 2 improbable. At the time of the high point of the diurnal variations in pressure the anterior chamber is deeper than at the time of the low. This permits the interpretation that at the time of the high pressure the eye contains more aqueous than at the time of the low. During the ascent the aqueous is regenerated more rapidly than during the low. No hyperemia of the ciliary body or of the iris was noted during the ascent. Determinations of the ocular rigidity did not indicate hyperemia of the posterior segment. We believe the evidence presented suggests that normal production of intraocular fluid exceeds the capacity of the channels of outflow and is the mechanism underlying the morning rises of intraocular pressure observed here. About noon this production stops or becomes reduced to a rate not exceeding the capacity of the outflow channels, whereby the latter are given an opportunity to catch up.

904 West Adams Street

RETROLENtal FIBROPLASIA IN PREMATURE INFANTS

V FURTHER STUDIES ON FIBROPLASTIC OVERGROWTH OF PERSISTENT TUNICA VASCULOSA LENTIS

T L TERRY, M D

BOSTON

Since the last reports¹ on retrorenal fibroplasia, sufficient further data have been collected to warrant another communication.

At the time of writing the number of cases registered in this study is 105. In Chicago 20 more have been observed by Dr E V L Brown and Dr Justin Donegan and an additional 20 by Dr Sanford Gifford.² Dr Milton Little,³ of Hartford, Conn., has at least 15 infants with retrorenal fibroplasia under his care. Dr Stewart Clifford,³ of the pediatrics staff of the Boston Lying-In Hospital, found that the disease occurs in 12 per cent of infants weighing 1,307 Gm (3 pounds) or less at birth, but since this percentage is based on less than 50 patients it is not necessarily representative.

In the cases in this study it has been observed that when no complications arise the opaque tissue making up the retrorenal fibroplasia usually becomes less dense, so that in places a red reflex can be obtained and in some instances the fundus can be observed in detail. Although this improvement may represent resolution and liquefaction of this opaque tissue, it is more reasonable to presume that the embryonic connective tissue contracts as it matures. As it contracts, its anteroposterior thickness is reduced and may tend to shred, giving rise to spaces, or meshes, through which one can see the details of the fundus. It is obvious that when this occurs the opaque tissue does not form a thin membrane behind the crystalline lens only but tends to invade the entire vitreous humor.

Read at the Eightieth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 31, 1944.

1 Terry, T L. Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants (a) I Preliminary Report, Am J Ophth 25: 203 (Feb) 1942, (b) II Report of Cases, Arch Ophth 29: 36-53 (Jan) 1943, (c) III Embryological Studies, Am J Ophth 25: 1409-1423 (Dec) 1942, (d) IV Etiologic Factors, Arch Ophth 29: 54-68 (Jan) 1943.

2 Terry, T L. Ocular Maldevelopment in Extremely Premature Infants. Retrorenal Fibroplasia, Bull Hist Med, March 1944.

3 Personal communication to the author.

The edges of the opaque tissue may appear sharp, but usually when viewed with a slit lamp the fibrillae are gradually reduced in number and density and finally disappear, like the edge of a fleecy cloud. Of course, the apparent reduction in the amount of opaque tissue, which is usual, could result from growth of the eye without growth of the fibroplastic tissue, but this seems unlikely, since eyes affected with retrorenal fibroplasia usually grow slowly, if at all. The apparent resolution rarely develops sufficiently to permit good vision. A posterior cortical cataract may develop, however, and increase the opacity, so that the blood vessels in the fibroplastic tissue become obscured. In some instances there is dramatic clearing of the opaque tissue in the vitreous humor, and it is evident that a considerable amount of vision is present. This improvement is most obvious in eyes which have grown appreciably and have anterior chambers of nearly normal depth. When a bright red reflex can be seen and the details of the fundus made out, retinoscopic examination is performed. The eyes of 2 infants were found to be extremely hypermetropic, those of 1 were myopic. In 2 instances glasses were prescribed, these the children tolerated well.

With favorable development, the searching nystagmus, so typical early in the disease, tends to abate and even disappear, and internal strabismus develops frequently. In most of the patients the improvement has been only moderate. Although it is apparent that infants with this condition are conscious of light stimulation and that some of them see relatively large objects which present a great contrast, there is no evidence of ability to judge distance, because these infants never reach for the objects, as do seeing infants of the same age. In an attempt to determine whether or not the fovea had developed and was functioning even moderately well, the parents were asked to use two or three different colored lights, each having a specific meaning—indicating feeding time, bath time and rest time—and to vary the schedule sufficiently so that the color of the light would

eventually establish a conditioned reflex. This failed, but the failure may have been a matter of improper establishment of the conditioned reflex rather than an indication that perception of color was entirely lacking. If it were possible to show that discrimination of color is present, the prognosis would be better.

All Caucasian infants born prematurely and observed soon after birth in this study have had a gray-blue iris. For this typical color I have used the term "fetal blue." In cases in which the eyes grow rapidly and the depth of the anterior chambers becomes relatively normal, this fetal blue color is quickly lost, but even in the most severely involved eyes, which grow little or none, there is eventually a definite, but incomplete change of color. In brunet infants the iris becomes an abnormally dull brown.

As only 3 of the patients showed mental abnormalities at this early date, there seems to be no correlation between retrothalental fibroplasia and retardation in mental development of premature infants. Mental retardation does occur in about 10 per cent of all premature infants.⁴

Of the cases originally reported,^{1b} case 7 must be disregarded. Pathologic examination of the left eye gave evidence that an unyielding tissue had pulled the retina and optic nerve toward the crystalline lens, thus indicating the method by which retinal folds and retinal separations originate in retrothalental fibroplasia. Although this may still be a true concept of how retinal separation develops in many of the infants with typical fibroplasia the reason for removing this case from consideration is that a younger sister of the patient in this case, born at full term, had the same type of ocular disease as observed clinically in case 7. This must, then, represent a hereditary defect of the eye. The prematurity of the older child was the factor which led to the original inclusion of her case in this study.

In the cases in this series the eyes of the infants which were treated with roentgen rays showed no benefit. Dr. Pelham Glover,³ of Altoona, Pa., had 2 patients whose eyes he felt improved after implantation of radon seeds. A repetition of his treatment was given in 2 cases in this series; in both instances the eyes not only showed no improvement but exhibited typical phthisis bulbi.

It has already been pointed out that at birth all extremely premature infants have a functioning tunica vasculosa lentis. The venous drainage for this vascular system is through the pupillary

portion of the tunica vasculosa lentis, the so-called pupillary membrane, to the anterior surface of the iris. In all infants, including those in whom retrothalental fibroplasia later developed, the pupillary portion of the tunica vasculosa lentis, as seen grossly, undergoes involution. It is possible, however, for small vessels of about the size of a capillary to persist at the extreme edge of the pupillary margin of the iris, thus furnishing an invisible drainage for the still functioning tunica vasculosa lentis. It is possible, and even probable, that in some cases the tunica vasculosa lentis behind the pupillary membrane persists without any venous drainage, just as at times the hyaloid artery persists, ending blindly near the lens. As embryonic connective tissue can develop in the meshwork of the tunica vasculosa lentis behind the crystalline lens, so also connective tissue elements may develop around these blood vessels. This new tissue would be inflexible and unyielding and bind the pupil down at these points, and this would give rise to posterior synechia. Before the appearance of the fibroplastic overgrowth, however, the blood vessels circling the pupillary margin were delicate and elastic enough to permit normal dilation and contraction of the pupil. Posterior synechia does develop frequently in infants with retrothalental fibroplasia without any evidence of an inflammatory process. Development of fibroplastic tissue around these blood vessels would account, in part at least, for the persistence of the fetal blue or the dull brown color of the irides.

Development of glaucoma is common enough to warrant careful attention; 5 cases have been observed. This does not necessarily mean that the eyes in these cases produce aqueous humor in sufficient amounts to induce this complication. Lack of development of the meshwork of the iris angle and Schlemm's canal would induce glaucoma even where there is an extremely small production of aqueous humor. In these 5 cases the eyes remained microphthalmic. In only 1 instance, a case which Dr. Georgiana Theobald brought to my attention, was hydrocephalus present. A 1 per cent solution of pilocarpine nitrate was used daily in these cases in an attempt to prevent the development of glaucoma, and no new cases have occurred. Examination of the few pathologic specimens of retrothalental fibroplasia showed a poorly developed meshwork of the iris angle. It seems reasonable to presume that hydrocephalus would invariably arise in these cases if aqueous humor were elaborated in sufficient amounts.

It has already been pointed out that there is a strong tendency toward the development of

⁴ Rosenoff and Inman-Kane cited by Hess, J. Mohr, G. J., and Bartelme, P. F. *The Physical and Mental Growth of Prematurely Born Children*, Chicago University of Chicago Press, 1934, p. 151.

posterior synechia. In an attempt to prevent this, a mydriatic⁵ which is effective for only a few hours was used once each week. This prophylactic measure has been less successful in preventing posterior synechia than that used to prevent glaucoma. The effectiveness of these treatments can be determined only through further study. The infants soon resist the use of all collyria as energetically as they can, and such medication is to be avoided when it is really safe to do so. Nevertheless, I have not felt justified in giving it up until either the failure of prophylaxis has been proved or the eyes have shown definite evidence of growth and a deepening of the anterior chamber.

Continued clinical study of this disease has shown that one of the physical findings was incorrectly interpreted. The toothlike processes at the periphery of the opaque tissue were originally called "dentate processes" or "gothic arches." These were thought to represent a serration at the edge, resulting from the insertion of the opaque tissue in the ciliary processes. It was noted that these arches, presumed to correspond to the ciliary valleys, were usually red like the normal fundus reflex. Sometimes they were dark brown, a color not feasible on the basis of the original interpretation. In 1 recent case, observed when the infant was under ether anesthesia and with the pupil fully dilated, a transilluminator was applied to the sclera for the purpose of determining whether or not a massive intraocular hemorrhage had occurred—a complication that has arisen in some cases. The eye transilluminated well, and from one side a clear view was obtained of this region of "dentate processes." It was obvious at a glance that these red or dark brown areas were in reality the ciliary processes themselves, with the opaque connective tissue of the fibroplasia extending behind them. A study of the ciliary processes under these conditions showed that there was considerable variation in the amount of pigment in this organ. In some cases the processes were red at their extremities, but nearer their bases there was a gradual change to dark red and then to the dark brown of the normally pigmented processes.

The eyes of 2 patients who did not have fibroplasia were examined while they were under ether anesthesia. One had unilateral micro-

thalmos and the other retinoblastoma. It was possible to see the ciliary processes through dilated pupils, even though the anterior chambers were of normal depth (figs 1 and 2A). In spite of blue irides, the processes were dark brown and fully twice as wide as those in infants with fibroplasia. In an infant of 4½ months with retrolental fibroplasia, which was absent in one quadrant, the ciliary processes were longer and narrower in the region where the fibroplasia

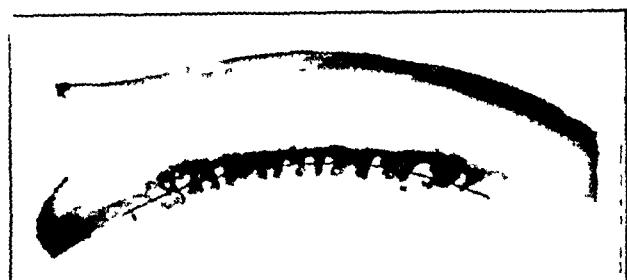


Fig 1.—Adult human ciliary processes as seen in an "end piece" removed when the globe was opened for microscopic sectioning. A portion of the cornea which has been cut through obliquely is seen. Note the relation of width of the ciliary processes to that of the ciliary valleys. The black line indicates the extent to which the tips of the processes can be seen through the dilated pupil in a newborn infant's eye.

was most noted (fig 2B). The ciliary processes were wider and shorter in the quadrant where fibroplasia was lacking (fig 2A). The ratio of the width of the ciliary processes to the width of the intervening ciliary valleys was 1.3 in the region of fibroplasia and 1.15 in the quadrant

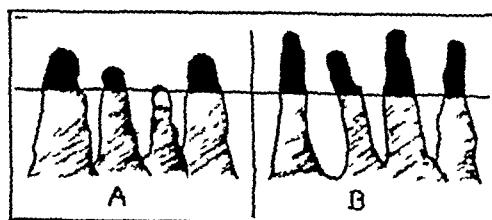


Fig 2.—Diagram showing variations in thickness and length of ciliary processes in (A) a normal infant eye and (B) an infant eye containing fibroplasia. The solid black tips represent the part visible in clinical examination with the ophthalmoscope or by means of transillumination. The appearance of the processes in A is consistent with the appearance of normal ciliary processes, as shown in figure 1.

where fibroplasia was lacking. If the wider, shorter processes represent the true appearance of normal ciliary processes, then those seen in fibroplasia, often appearing red or free of pigment, are indeed definitely undeveloped—strong evidence that the ciliary body is maldeveloped. A further study of ciliary processes at various times as the infants grow may prove of value in showing variation in rate of development, in pigmentation and in size.

	Gm
5 Homatropine hydrobromide	0.15
Epinephrine bitartrate	0.30
Cocaine hydrochloride	0.075
Paredrine hydrobromide* 1 per cent	15.000

*Parahydroxy- α -methylphenylethylamine
hydrobromide

The original concept, that the disease arose through hypertrophy of the intraocular vascular system because of a precociously high blood pressure resulting from premature birth, seems less tenable as the factors are examined more minutely. Thoma⁶ pointed out that the effect of increased blood pressure is to keep a vascular system open as well as to cause it to hypertrophy. This is indeed the case in instances of abnormal arteriovenous communication, in which the arteries, relieved of considerable pressure because of the fistula, atrophy and become vein-like, whereas the veins, now subjected to a pressure almost arterial in amount, hypertrophy and become artery-like. In addition, there is an actual increase not only in the width of the capillaries but in the number of capillaries in this bed.⁷ At no stage in normal development is the future need for blood vessels anticipated. The blood vessels, considered to be the most adaptable tissue in the embryo and fetus, are not developed at any stage of embryonic and fetal life beyond the needs of the organism at that time. Thus, the blood vascular system is constantly meeting the demand for oxygenated blood from the ever changing tissue as growth and development proceed. High blood pressure itself does not cause widespread new capillary growth, as might be expected from Thoma's hypothesis. The cornea becomes vascularized not because people have high blood pressure but because there is a local need for blood in response to an inflammatory process or an injury. If this reasoning can be used in relation to retro-lental fibroplasia with persistence of the tunica vasculosa lenticis and hyaloid artery, then the cause of the disease is not a precociously high blood pressure but lies in the fact that there is a need for this vascular system.

Of course, until the cause of this disease process is definitely known, all possible etiologic factors must be considered. In experimental work, attempts were made either to produce the disease or to cause a precocious involution of the hyaloid artery and the tunica vasculosa system in hundreds of opossums and young rats. Although the disease was not produced, repeated dilation of the pupil and examination

⁶ Thoma, cited by Keibel, F., and Mall, F. D. Manual of Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, p. 421.

⁷ Reid, J. R. Studies on Abnormal Arteriovenous Communications Acquired and Congenital, Report of Series of Cases, Arch. Surg. **10**, 601 (March) 1925, Origin and Nature of Arteriovenous Aneurysms, *ibid.* **10**, 996 (May) 1925. Effects of Abnormal Arteriovenous Communication, *ibid.* **11**, 25 (July) 1925, Treatment of Abnormal Arteriovenous Communication, *ibid.* **11**, 237 (Aug.) 1925, Am. J. Surg. **14**, 14, 1931.

of the eyes of these animals with an ophthalmoscope did tend to delay the time at which this vascular system disappeared. In the earlier study it seemed highly improbable that precocious exposure to light was an etiologic factor, especially in its effect on the retina per se, despite observation that the process of myelination of the optic nerve appeared to be accelerated in prematurely born infants.⁸ Consideration of the possible effect of pupillary response and even of accommodation in premature infants leads to a more plausible cause of the development of fibroplasia. The pupil does contract and dilate in an extremely premature infant in response to exposure to light and to use of a mydriatic, but the possibility of accommodative or other activity of the ciliary muscle is only theoretic.

It is probable that active pupillary responses could embarrass the venous drainage of the tunica vasculosa lenticis by stretching and tending to kink the vessels as they extend from the posterior surface around the pupillary margin to the anterior surface of the iris. Should this cause closure of the vessels at the pupillary margin, then perhaps the hyaloid artery and the tunica vasculosa lenticis would persist, with considerable passive congestion in them. Passive congestion in itself is not presumed to cause fibrosis, but the edema associated with it can produce fibrosis such as is seen in so-called pulmonary osteoarthropathy.⁹

Again, the pupillary response without, or more likely with, some muscular activity of the ciliary body may tend to open the meshwork of the iris angle. From the appearance of the ciliary body in the fetal eyes one can conclude that aqueous humor is formed before Schlemm's canal and the meshwork of the iris angle is developed sufficiently to take away any or all of this fluid and that this thus produces a higher intraocular pressure—a temporary physiologic "glaucoma." In fact, the mechanism by which congenital glaucoma develops may for a while be active in all eyes as a normal process, being relieved by the development of an adequate device for drainage of aqueous humor from the eye, a development which fails to occur in hydrocephalus. If the meshwork of the iris angle is opened in a form capable of physiologic activity through the pull of the uveal tract musculature on the scleral spur, then precocious exposure of the eye to light and optic imagery in a prematurely born infant would open the angle and drain aqueous

⁸ Salzman, M. The Anatomy of the Human Eye, translated by E. V. L. Brown, Chicago, University of Chicago Press, 1912, p. 208.

⁹ Wolbach, S. B. Personal communication to the author.

humor from the eye, thereby circumventing the occurrence of transitory physiologic glaucoma. This lack of aqueous humor would result in an extremely shallow anterior chamber and a decrease in intraocular pressure which would fail to stimulate growth of the eye, thus giving rise to microphthalmos. The crystalline lens and the cornea in part obtain their nutrition from the aqueous humor. If nutrition is inadequate, formation of cataracts and corneal opacities, which later occur in retroental fibroplasia, is explained. Until this aqueous humor is developed in the fetal eye these organs are nourished by the tunica vasculosa lentis system. If aqueous does not develop, then the need for nourishment of the lens and cornea could be supplied by persistence of the hyaloid artery and tunica vasculosa lentis. Thus, lack of accumulation of aqueous humor explains many but not all of the findings in retroental fibroplasia, the occasional occurrence of glaucoma as a complication needs some further explanation.

Another view is that the ciliary body fails to elaborate aqueous humor. Whether the absence of formation of aqueous humor is the result of lack of permeability of the capillary walls and the ciliary epithelial layers separating the capillaries from the posterior chamber or of lack of an adequate vascular supply to the ciliary processes is purely conjectural. A microscopic study of the few specimens of fibroplasia available showed abnormal ciliary processes in the disease. These were distorted and stretched out but not connected to the fibroplastic mass in every case. Thus, morphologic evidence of abnormality of the ciliary body does exist.

If the ciliary body is at fault because of improper vascular development, it is probable that a more adequate vascular connection could be produced surgically. In considering these possibilities one recalls the proposal made by Sondermann¹⁰ regarding a certain type of glaucoma. He stated the belief that glaucoma could arise from overproduction of aqueous humor in relation to increasing stricture of the vortex vein at the region of the ampulla and substantiated this theory with pathologic specimens. Sondermann said that such glaucoma could be detected by observing fluorescein sodium in the anterior chamber in an extremely short time after an intravenous injection, as compared with the time for a normal eye. He expressed the opinion that there is occasionally a "secretory" glaucoma. He attempted to establish new vascular drainage

of the ciliary body by performing a trephination of the sclera over the ciliary body, so that the scar tissue repair of this lesion and the newly formed blood vessels along this tract could connect the circulation of the ciliary body with that of the episclera. In Sondermann's hands this operation has been effective. Provided a better arterial blood supply or a better venous drainage of the ciliary body is needed and can be surgically established, it is possible that this type of operation could be of value in retroental fibroplasia.

After careful consideration of possible complications, this operation was tried on 1 infant who had unilaterally a marked persistence of functioning pupillary membrane, a shallow anterior chamber, a fetal blue iris and an opacity deep in or behind the crystalline lens. Three weeks after the operation the blood vessels in the pupillary membrane had ceased functioning, the color of the iris improved, the anterior chamber deepened and the eye was growing—a dramatic result. Similar operations have been performed on 18 infants. In 2 the eyes showed so much improvement that each mother requested that the operation be done on the other eye also. Six other eyes have shown improvement after this operation. In 1 patient glaucoma was relieved and did not recur. If the operation is really responsible for the improvement, it is possible that the benefit may be derived from some factor in the operation not now obvious. This operation may have possible therapeutic value for these infants, but this statement is made with hesitation, since the operation has yet to prove its value. In this series, however, no complications have arisen. It should by no means be performed routinely on all infants with retroental fibroplasia until it has proved its worth in carefully selected cases, in which there is little chance of harm and great chance of improvement. This method of determining the effectiveness of surgical treatment must necessarily be slow, especially when it is considered that many of the eyes operated on show considerable deterioration and would not improve even after an operation of proved value.

The justifiable indications for an operation on such an insecure basis have been in infants with one eye severely involved and the other eye showing little or no involvement or in infants with severe bilateral fibroplasia in whom a complication such as glaucoma, formation of posterior synechia, or development of corneal opacities or a combination of these is beginning to appear.

The technic of the operation is as follows. The conjunctival flap is turned down toward

¹⁰ Sondermann, R. Meine Glaukontheorie und die Klinik des Glaukoms, *Klin Monatsbl f Augenh* **92**, 313-335, 1934, A New Operation for Glaucoma, *Ber u d Versamml d deutsch ophth Gesellsch* **50** 78-81, 1934.

the limbus from about 4 mm behind. Care is taken to cleanse the sclera thoroughly, a 1 mm trephine is applied approximately 2 mm from the limbus. In eyes in which there is practically no anterior chamber, the danger of entering the iris angle is small. In no operation has this happened. A reduction in resistance is usually noted when the sclera has been completely penetrated, but inspection from time to time is the safest guide to knowing when one is approaching the ciliary body. The button is easily removed by gentle dissection, and the flap is replaced. The wound is reclosed with a continuous suture, the lower end of which is left relatively long, so that it can be easily removed without giving another anesthetic. No dressing

between the interior and the exterior of the eye if the need is strong enough.

SUMMARY

In approximately 12 per cent of all premature infants weighing 3 pounds (1,307 Gm) or less at birth retrobulbar fibroplasia develops.

Partial resolution of the fibroplastic tissue in the eyes in which growth does occur when no complications arise rarely results in improvement sufficient to permit good vision.

Occasionally, cataractous development may obscure deeper ocular changes.

Inability of the infants to judge distance is a common characteristic.

The "fetal blue" color of the iris persists longer, its speed of disappearance being in direct proportion to the rapidity of growth of the involved eye.

One atypical case originally reported must now be excluded. The full term birth of a younger sister with the same lesion indicated a probable hereditary factor, not evident in any other cases.

Mental retardation in infants with retrobulbar fibroplasia appears to be less frequent than mental retardation in normal premature infants.

Radiation therapy has proved to be valueless, in fact, more damaging than beneficial.

Glaucoma, a complication of some frequency, rarely gives rise to hydrocephalus and appears to be preventable by daily use of miotics. On the other hand, mydriatics having an effect of short duration used once a week are less successful in preventing posterior synechia.

The "dentate processes," originally improperly interpreted, are actually brown (pigmented) or red (unpigmented) ciliary processes, observable through dilated pupils, extending in front of the opaque tissue. These processes in infants with fibroplasia are narrower, often less pigmented and perhaps more elongated than the ciliary processes observed in the same manner in infants with normal eyes.

The more tenable theory of the cause of this disease is that failure of production or accumulation of aqueous humor may be caused by the effect of precocious exposure to light, which activates the musculature of the pupillary and the ciliary body before the hyaloid vascular system has disappeared. This failure leaves the crystalline lens dependent on the hyaloid artery and tunica vasculosa lentis, thereby causing persistence of this vascular system.

Surgical attempt to establish new vascular connections between the ciliary body and the episclera by scleral trephination over the ciliary body appears to produce some improvement.

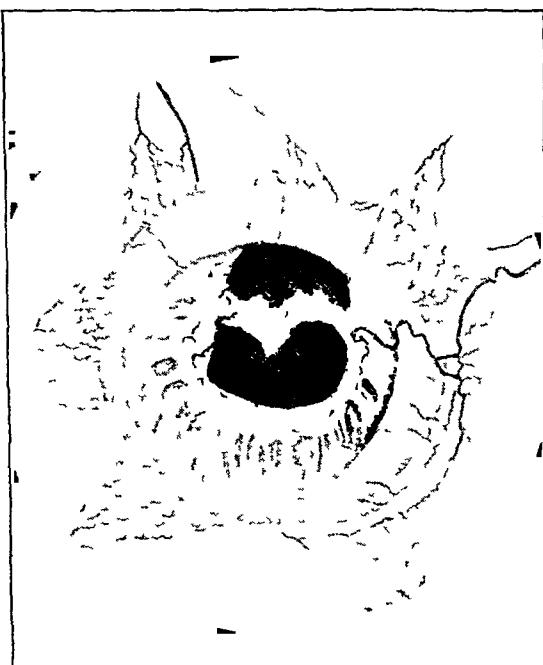


Fig. 3.—Artist's drawing of an eye in which the vascular connection between the iris and the episcleral net extends along the scar of an incision made for extraction of a cataract. This shows that if need for a newly formed vascular connection exists such a connection can be established along an operative wound.

is applied to the eye, and on the fifth day the suture is removed.

No eyes that have had this operation performed on them have been obtained, it is impossible to state whether or not new vascular connections are actually produced. In 1 instance however, I have seen a vascular connection between episcleral vessels and newly formed vessels on the iris along the tract of an incision made for extraction of a cataract in a patient with severe glaucoma (fig. 3). This demonstrates that new vascular connections large enough to be seen without magnification can be and are established along an operative wound.

TWO UNUSUAL OCULAR TUBERCULOMAS

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The rarity of primary tuberculosis of the bulbar conjunctiva justifies the description of a case of this condition. The second case described in this article is an instance not of primary tuberculosis but of the formation and spread of a tuberculoma which are unusual and worthy of record.

The incidence of primary tuberculosis of the conjunctiva varies from 1/3,000 to 1/60,000 cases, of which 20 to 30 per cent are instances of the bulbar variety¹. It is difficult to ascertain whether a tuberculous focus is primary or not. It is a general rule, originating from Axenfeld,² that progressive pulmonary tuberculosis is antagonistic to the establishment of tuberculosis in the eye. The cutaneous reaction to tuberculin is not entirely specific or dependable, for in some cases of proved tuberculosis the reaction is negative and a positive cutaneous reaction has been described in some cases in which no tuberculosis was present.³ In our opinion, a positive reaction to an intradermal test with 1/5,000 dilution of old tuberculin is still a useful indication of the state of allergy or anergy of a person. A further useful sign is that with primary conjunctival tuberculosis there is usually early involvement of the regional lymph glands.³ A few diagnostic signs in our first case point to the fact that the tuberculoma of the conjunctiva was primary in origin.

REPORT OF CASES

CASE 1—A South African Negro 25 years of age was admitted to the hospital with a note from his physician which stated that the patient while hammering on rock during gold-mining operations sustained a horizontal laceration of the bulbar conjunctiva three weeks before we saw him. A tumor developed over the site of injury, and because there was enlargement of the preauricular and premasseteric lymph glands, his physician thought it might be malignant. On examination there was found a roll-like, somewhat pedunculated, red tumor lying horizontally below the cornea.

1 Samuelson, A Primary Tuberculosis of Conjunctiva, *Arch Ophth* **15**: 975 (June) 1936.

2 Wegner, W *Zeitfragen der Augenheilkunde*, Stuttgart, Ferdinand Enke, 1938, p 328.

3 Igersheimer, J, in Schieck, F, and Bruckner, A *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1932, vol 7, p 87.

and attached to the scleral conjunctiva (fig 1). It was vascular, resembling a glaucoma, and the conjunctiva around it was moderately hyperemic. The surface of the tumor was smooth, and no sign of ulceration existed. The premassesteric and preauricular lymph nodes were enlarged, hard and painful when palpated. On attempting to remove a piece of the tumor for histologic examination, we found that the entire tumor could be torn off at its base. The raw area, where it had been attached, was cauterized by heat, and it healed without any untoward reaction. The lymph glands were left untouched. Histologic examination revealed that the biopsy material consisted of tuberculous granulation tissue, and an intradermal test with a 1/5,000 dilution of old tuberculin was immediately carried out.



Fig 1—A primary tuberculoma of the bulbar conjunctiva.

This was repeated a week later. Both tests gave negative results. A biologic test with material from the preauricular lymph gland gave positive results. Roentgenologic examination of the lungs and investigation of the sputum yielded nothing of importance. During the fifth week after the patient was admitted to the hospital the intradermal test with old tuberculin gave a strongly positive result. At no time was there a rise in temperature or any loss of weight. The patient was treated with a tubercle endotoxoid prepared by the method of Grasset.⁴ During the two months of endotoxoid treatment⁵ the enlargement of the pre-

4 Grasset, E *Tubercle Endotoxoid in the Treatment of Tuberculosis in South African Natives*, Am Rev Tuberc **49**: 1, 1944.

5 A full consideration of our results with tubercle endotoxoid treatment in ophthalmology will be the subject of a publication in the near future.

sesteric and preauricular glands slowly disappeared. The patient was discharged as cured after three months in the hospital.

In this case primary infection of the bulbar conjunctiva entered through a conjunctival wound. As this South African native is a worker in a gold mine, where he is exposed to tuberculous infection, such an entrance of the bacillus is feasible.

CASE 2.—In a South African Negro, approximately 40 years of age, a large, smooth, flattish, rounded tumor developed subconjunctivally on the sclera under the upper eyelid (fig. 2). It is not known how long this growth had existed before his physician discovered it. The tumor caused no vascular reaction in the overlying conjunctiva. The eye itself showed signs of long-standing chronic iridocyclitis, posterior synechiae and abundant keratic precipitates were present. Gonioscopically we could find only abnormal deposition of fine brown pigment on the iridocorneal trabecula and deposition of fibrinous masses central to the internal corneal bulge of Schwalbe. The lens was slightly hazy, but the vitreous was so cloudy that only an indistinct glimpse of the choroid of the lower quadrants of the fundus could be obtained. Roentgenologic and laboratory investigations gave negative results, there was mild lymphocytosis, and an intradermal test with 1:5,000 dilution of old tuberculin gave strongly positive results. Biopsy was thought necessary. Through a small conjunctival incision, a piece of the granuloma was excised, and at once vitreous humor appeared at the site. The conjunctiva was immediately sutured. It was now obvious that the vitreous protruded beyond its normal limits because of erosion of the coats of

the eye. During the three weeks following the operation the eye became inflamed and hypotonic, owing to advanced destruction of the uvea and reaction resulting from operative intervention. We instituted endotoxoid treatment, but it was already too late. After three weeks in the hospital the patient refused further treatment and at his insistence was repatriated to Portuguese East Africa. The pathologist reported that in the tuberculous granulation mass traces of choroid and sclera were present. No biologic test was made.



Fig. 2.—Subconjunctival protrusion of a uveal tuberculoma.

This tuberculoma could not have been primary in origin but must have been a blood-borne infection from some unknown source. What is interesting is the fact that the tumor eroded the coats of the eye and grew outward under the conjunctiva.

INTRAVITREAL PENETRATION OF PENICILLIN AND PENICILLIN THERAPY OF INFECTIONS OF THE VITREOUS

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With the TECHNICAL ASSISTANCE OF MARJORIE WILFIS, B A

PHILADELPHIA

Recently von Sallmann, Meyer and Di Grandi¹ have pointed out the unsatisfactory response of ectogenous infections of the vitreous to any type of therapy. Von Sallmann² demonstrated that iontophoresis with penicillin and iontophoresis plus systemic administration of sulfonamide compounds failed to produce improvement of ectogenous intraocular infections. Because these authors were unable to produce adequate levels of penicillin in the vitreous of the normal eye by corneal iontophoresis or by systemic administration, they resorted to direct intravitreal injections. Their studies showed that penicillin was present in the vitreous humor in a concentration greater than the bacteriostatic requirement for twenty-four hours after the initial injection. Initial intravitreal injections of penicillin produced retinal damage at the site of the needle puncture and opacities and occasional hemorrhage in the vitreous. The authors stated that if a fine needle was used and directed into the central area of the vitreous there was little danger of producing a cataract or retinal detachment with one injection of refined penicillin.

Von Sallmann, Meyer and Di Grandi¹ did not study the histologic damage following intravitreal injection of sulfonamide compounds. Leopold and Scheie³ briefly reported such changes following intravitreal injection of sulfanilamide, sulfapyridine and sulfathiazole. The histologic

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The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

1 von Sallmann, L., Meyer, K., and Di Grandi, J. Experimental Study on Penicillin Treatment of Ectogenous Infection of Vitreous, Arch Ophth 32:179 (Sept) 1944

2 von Sallmann, L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch Ophth 30:426 (Oct) 1943

3 Leopold, I. H., and Scheie, H. G. Studies with Microcrystalline Sulfathiazole, Arch Ophth 29:811 (May) 1943

damage brought about by such injections was similar to that observed with penicillin and was most pronounced with sulfapyridine. Leopold and Scheie³ suggested that there was little to be gained by intravitreal injections of sulfonamide compounds, as theoretically quite adequate concentrations in the vitreous could be obtained in infected eyes by systemic administration of these substances. They suggested that the only gain from such treatment would be an immediately high intravitreal concentration of the agent. The failure of intravitreal injections of the sulfonamide compounds to be more effective than the systemically administered drug in clearing infections with *Staphylococcus aureus*, as reported by von Sallmann, Meyer and Di Grandi,¹ substantiates this impression. These authors were able to halt the progress of infections of the vitreous with a hemolytic strain of *Staph aureus* by means of one intravitreal injection of a solution of penicillin. As already pointed out, their reasons for adopting this method of therapy were based on the inadequacy of concentrations in the vitreous obtained in the normal eye with less damaging routes of administration. It seemed advisable, therefore, to determine the vitreous concentrations to be obtained in the inflamed eye by intramuscular, intravenous and subconjunctival injections and by injection into the anterior chamber.

It is to be expected that with increased permeability of the capillaries there might be an increased penetration of penicillin into the vitreous. An increase in the secondary aqueous has been shown to follow systemic administration of penicillin after paracentesis by von Sallmann and Struble and Bellows⁴ and after inflammation by Leopold and LaMotte⁵.

4 Struble, G. E., and Bellows, J. G. Studies on the Distribution of Penicillin in the Eye, J A M A 125:685 (July 1) 1944

5 Leopold, I. H., and LaMotte, W. O., Jr. Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, Arch Ophth 33:43 (Jan) 1945

PENETRABILITY OF PENICILLIN INTO
THE VITREOUS

Methods of Administration.—The following routes of administration were considered in this study

1 Subconjunctival injection consisting of 0.25 cc of a solution containing 10,000 Oxford units of sodium penicillin per cubic centimeter⁶ of isotonic solution of sodium chloride U S P. Such injections were made in eyes previously anesthetized with a 0.5 solution of tetracaine hydrochloride.

2 Intramuscular injection of 4,000 Oxford units of sodium penicillin per kilogram of body weight

3 Intramuscular injections of 4,000 Oxford units of penicillin⁷ per kilogram of body weight. This solution of penicillin also contained naphthylmethylimidazoline hydrochloride,⁸ 0.25 mg per cubic centimeter, or neo-synephrine hydrochloride, 0.5 mg per cubic centimeter, and 20 or 6 per cent gelatin, the concentration depending on the vasoconstrictor used. Such preparations have been shown by Rhoads and his associates⁹ to maintain high levels of the substance in the blood for several hours. This method was tried here with the hope that the prolonged level of the substance in the blood would allow greater penetration into the vitreous humor.

4 Intravenous injections of penicillin. Each injection contained 4,000 Oxford units of the sodium salt per kilogram of body weight

5 Injections into the anterior chamber of 0.25 cc of a solution containing 2,000 units of sodium penicillin per cubic centimeter. The anterior chamber was punctured obliquely, starting at the limbus in eyes previously anesthetized with a 0.5 per cent solution of tetracaine hydrochloride. The aqueous humor was withdrawn into the syringe and mixed with the penicillin solution in the syringe. Then 0.25 cc of the mixture of penicillin solution and aqueous humor was injected into the anterior chamber. The resultant solution injected contained approximately 250 Oxford units of penicillin. Although the punctures were made obliquely through the cornea, some of the aqueous mixture leaked from the puncture site, so the exact amount in the anterior chamber was not known. All concentrations of penicillin were determined by a modification of Rammelkamp's method of bioassay.¹⁰

Studies were made on the following types of rabbit eyes:

1 Normal rabbit eyes

6 The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutics and other agents of the National Research Council.

7 This preparation of penicillin was supplied by Dr. William Parkins, of the Harrison Department of Surgical Research of the Hospital of the University of Pennsylvania.

8 This compound was obtained in the form of pravine hydrochloride (Ciba Pharmaceutical Products, Inc.)

9 Rhoads, J. E., and others. Personal communication to the author.

10 Rammelkamp, C. H. Methods for Determining Concentration of Penicillin in Body Fluids and Exudates. Proc. Soc. Exper. Biol. & Med. 51:95 (Oct.) 1942.

2 Rabbit eyes with infections of the anterior chamber. The infections were produced by injection of 0.02 cc of a diluted eighteen hour broth culture of a hemolytic strain of *Staph. aureus*. Each injection contained approximately 400 organisms. One could not be certain of the exact amount of culture retained in the anterior chamber, as some aqueous humor always leaked out of the puncture. However, in all eyes so treated signs of severe infection developed within twenty-nine hours, these eyes were anesthetized with a 0.5 per cent solution of tetracaine hydrochloride prior to injection of the culture. Penicillin studies were made twenty-four hours after such injections.

3 Rabbit eyes with 0.02 cc of histamine hydrochloride (1:1,000) injected into the vitreous fifteen minutes before administration of any penicillin preparation. All eyes were locally anesthetized with a 0.5 per cent solution of tetracaine hydrochloride.

4 Rabbit eyes on which basal iridectomies were done two weeks prior to any penicillin studies. Approximately one fifth of the iris was removed in this operation.

In all instances, the specimens of vitreous were analyzed fifteen minutes, forty-five minutes and one hour.

TABLE 1.—Intravitreous Concentrations of Penicillin Following Intramuscular and Intravenous Administration of Penicillin

Method of Administration	Time of Analysis After Administration, Min	Normal Eyes Oxford Units of Penicillin per Cc	Eyes with Infections of Anterior Chamber, Oxford Units of Penicillin per Cc	Eyes with Intra-vitreous Histamine, Oxford Units of Penicillin per Cc
Intramuscular, 4,000 units/Kg	15	0	0	0
	45	0	0.03	0
	105	0	0.03	0
Intramuscular, 4,000 units/Kg (+ gelatin and vasoconstrictor substance)	15	0	0	0
	45	0	0	0
	105	0	0.03	0.02
	180	0	0	0
	240	0	0	0
Intravenous, 4,000 units/Kg	15	0	0	0
	45	0	0.03	0
	105	0	0.07	0.02
	180	0	0.01	0

and forty-five minutes after the initial administration of penicillin. After some modes of administration it was necessary to determine the concentrations of penicillin in the vitreous three hours and four hours after injection.

Results.—The data are listed in tables 1, 2, and 3. All levels represent the average levels for the two eyes. It is evident from the data listed in table 1 that detectable concentrations of penicillin in the vitreous were not present in normal eyes after intravenous or intramuscular administration of penicillin. These results also indicate that prolongation of the level of penicillin in the blood by use of a penicillin-gelatin-vasoconstrictor preparation did not increase the penetration of penicillin into the vitreous of normal eyes. In eyes with infections of the anterior segment the penicillin did penetrate into the vitreous humor with all these methods. Intravenous injection produced the

highest levels of penicillin in the vitreous Penicillin in the vitreous was just detectable in eyes which had received intravitreous injections of histamine prior to administration of the penicillin

The results of subconjunctival administration of penicillin are recorded in table 2 Although the presence of the substance in the vitreous was detectable in normal eyes for three hours after such an injection, the levels were much

TABLE 2.—*Intravitreous Concentrations of Penicillin Following Subconjunctival Injections of Penicillin*

Time of Analysis After Injection, Min	Normal Eyes, Oxford Units of Penicillin per Cc	Eyes with Infection of Interior Chamber, Oxford Units of Penicillin per Cc
15	0.000	0.128
45	0.078	0.510
105	0.078	0.250
180	0.078	0.250

greater in eyes with an inflamed anterior chamber Even in normal, as well as in inflamed eyes subconjunctival injection produced higher intravitreal levels than the intramuscular or the intravenous mode of administration

The results of injections into the anterior chamber are presented in table 3 The concentrations in the vitreous of normal eyes were greater than the concentrations obtained by any previous method The levels obtained in inflamed eyes were still greater In eyes which were normal except for previous iridectomy, the vitreous level exceeded that in the vitreous of normal eyes similarly treated with injections into the anterior chamber

TABLE 3.—*Intravitreous Concentrations of Penicillin Following Injections of Penicillin Into Anterior Chamber*

Time of Analysis After Injection, Min	Normal Eye, Oxford Units of Penicillin per Cc	Eyes with Infection of Anterior Chamber, Oxford Units of Penicillin per Cc	Eyes with Iridectomy, Oxford Units of Penicillin per Cc
15	0.312	0.624	0.312
45	0.312	1.200	0.312
105	0.312	0.624	0.624
180	0.078	0.312	0.312
240	0.039	0.078	0.624

In a recent review, Salter¹¹ has indicated that a desirable concentration of penicillin in the blood would be in the range of 0.15 Oxford unit per cubic centimeter Theoretically, therefore, all the methods described which produce intravitreous levels in excess of 0.15 Oxford

11. Salter, W T Antibiotics and Bacteriostatics in Blood and Body Fluids, New England J Med 231: 651 (Nov 9) 1944

unit per cubic centimeter might be of value in treating infections of the vitreous due to penicillin-sensitive organisms The methods which produce levels of 0.15 Oxford unit per cubic centimeter of vitreous or higher in infected eyes merit trial in treatment of infections of the vitreous Subconjunctival injection and injection into the anterior chamber produced levels in the vitreous above 0.15 unit per cubic centimeter in eyes with an inflamed anterior segment The parenterally administered penicillin never reached this concentration in the vitreous Intravenous administration of penicillin produced a concentration of penicillin in the vitreous of about 0.08 unit per cubic centimeter in the inflamed eye This was the highest level reached with the parenteral method of administration These methods were therefore compared with the intravitreal injection of penicillin for effectiveness in combating an experimental ectogenous infection of the vitreous

PENICILLIN THERAPY OF INFECTIONS OF VITREOUS

Method—All rabbits were of a blue-eyed or brown-eyed chinchilla strain, weighing between 2 to 3 Kg The organism used was *Staph aureus*, taken from a patient with septicemia An eighteen hour culture of this organism was sensitive to concentrations of penicillin in the serum ranging from 0.05 to 0.02 Oxford unit per cubic centimeter Intravitreous injections of 0.01 cc of a diluted eighteen hour broth culture of this organism were made in both eyes of 50 rabbits Each injection contained approximately 400 organisms In all eyes receiving such injections signs of severe infection developed in twenty-four hours By that time aqueous flare and floaters were conspicuous The vitreous gradually became opaque, preventing any detailed view of the fundus All untreated eyes were phthisical after four to six weeks Treatment was started in all rabbits two hours after injection of the culture of *Staph aureus* The following methods of treatment with sodium penicillin were used

1 Intravenous administration of 4,000 Oxford units of penicillin per kilogram of body weight Injections were made every two hours and were continued for seventy-two hours Six rabbits were used

2 Subconjunctival injections of 0.25 cc of a solution containing 10,000 Oxford units of penicillin per cubic centimeter These injections were made every three hours for seventy-two hours The previous determinations of intravitreal concentrations indicated that one such injection maintained concentrations above 0.20 Oxford unit per cubic centimeter for three hours The right eyes of 6 rabbits were so treated, the left eyes receiving no therapy

3 Injections into the anterior chamber of 0.25 cc of a solution containing 2,000 units of penicillin per cubic centimeter These injections were made in a manner similar to the injections described in the first part of this paper According to the intravenous levels of penicillin obtained, one such injection maintained the intravitreal concentration of penicillin above 0.3 Oxford

unit for three hours. Therefore injections were made every three hours. Although care was exercised not to touch the lens with the needle, considerable damage to the lens occurred in 3 eyes so treated. Occasional hemorrhage occurred in the anterior chamber, and considerable fibrinous exudate appeared in all eyes, which made repeated injections difficult and inconstant in amount. This method of therapy was continued for seventy-two hours. The right eyes of 6 rabbits were so treated, the left eyes receiving no therapy.

4 Intravitreal injections of 0.25 cc of a solution of penicillin containing 10,000 Oxford units per cubic centimeter of isotonic solution of sodium chloride. The cornea became hazy after each such injection, owing to the increase of intraocular tension, but cleared within a short while as some fluid leaked from the puncture site. All injections were made after anesthetizing the eye with a 0.5 per cent solution of tetracaine hydrochloride. These injections were made into the center of the vitreous, care being taken to avoid making contact with the lens. The right eyes of 6 rabbits were so treated, the left eye of each animal receiving no therapy.

5 Intravitreal injections of penicillin of various concentrations. Two right eyes received 2,000 units per injection, 2 right eyes, 1,000 units per injection, 2 right eyes, 500 units per injection, 2 right eyes, 250 units per injection, 4 right eyes, 100 units per injection, 2 right eyes, 50 units per injection, 2 right eyes, 25 units per injection, 2 right eyes, 10 units per injection, and 2 right eyes, 5 units per injection. All 20 left eyes received no therapy and acted as controls.

6 Injections into the anterior chamber of 0.25 cc of isotonic solution of sodium chloride. Injections were made in six right eyes every three hours for seventy-two hours.

7 Intravitreal injection of 0.25 cc of isotonic solution of sodium chloride. One injection was made in each of 6 eyes.

Results of Therapy.—All the 38 left eyes which received no therapy showed pronounced softening and opacity of the vitreous in four weeks. The 6 eyes which received injections of isotonic solution of sodium chloride into the anterior chamber and the 6 eyes which had intravitreal injections of isotonic solution of sodium chloride also were phthisical after four weeks of observation. All 12 eyes treated with intravenously administered penicillin showed all the signs of phthisis bulbi after four weeks. Four of the eyes which received subconjunctival injections appeared similar to the control eyes, while 2 of these eyes showed posterior cortical opacities of the lens, prominent opacities of the vitreous and a partial view of the fundus after four weeks. The inflammatory process was arrested in these 2 eyes, but no further clearing occurred in the subsequent ten weeks of observation. One of the eyes treated with injections into the anterior chamber showed only a few vitreous and lenticular opacities and most of the fundic details could be seen after four weeks. One eye so treated allowed a partial view of the fundus. Posterior synechiae

were present in this eye, as well as lenticular and large vitreous opacities. The intraocular tension, however, was maintained. The remaining 4 eyes showed phthisis bulbi at the end of four weeks.

All 6 eyes treated with injections of 2,500 Oxford units of penicillin were quiet after four weeks of observation. Occasional opacities in the vitreous, but no other sign of inflammatory activity, could be seen in all the eyes. Of the 20 eyes treated with decreasing doses of penicillin by injection into the vitreous, all receiving more than 1,000 units per injection were favorably influenced, in a manner similar to the eyes treated with 2,500 units per injection.

One eye each of the eyes receiving injections of 500 and 250 units into the vitreous also appeared similar to the eyes receiving 2,500 units per injection. All the remaining eyes showed considerable opacification of the vitreous, lenticular opacities and posterior synechiae. A partial view of the fundus could be obtained in these eyes, and the intraocular tension was maintained in the other eye which received 250 units in 2 of the 4 eyes which received 100 units and in 1 each of the eyes receiving 50, 25, 10 and 5 units per injection. Even in the poorest of the last-mentioned eyes the inflammatory process was never as severe, nor did the eyes progress as rapidly to the end stages, as in the untreated controls.

COMMENT

It is evident that subconjunctival injection and injection into the anterior chamber will produce theoretically adequate concentrations of penicillin in the vitreous in inflamed rabbit eyes. Administration of 4,000 units of penicillin per kilogram by the intravenous or by the intramuscular route does not. When these methods are tried against a standard ectogenous infection of the vitreous produced by a highly susceptible strain of *Staph aureus*, subconjunctival injection of penicillin and injection into the anterior chamber have some success in combating the infection. This success is not striking even when therapy is started two hours after inoculation of the vitreous with the organisms. Intravitreal injections were successful in all cases when the concentration of penicillin was above 500 Oxford units per injection. Even lower concentrations, as small as 5 Oxford units per injection, had some effect. Thus intravitreal injections are superior in therapeutic efficiency to subconjunctival injection and injection into the anterior chamber. However, both methods have some

merit, whereas all methods of systemic administration fail entirely.

Injections into the anterior chamber in themselves produce considerable disturbance in the aqueous. Dunnington and von Sallmann¹² showed that one such injection produces reparable changes. However, repeated injections of penicillin produced some irreparable damage in the present experiments. Lenticular opacities and anterior and posterior synechiae occurred. Much of this damage may be mechanical in origin, as the eyes which received repeated injections of isotonic solution of sodium chloride into the anterior chamber also showed lenticular damage and formation of synechiae. However, iontophoresis² and subconjunctival injections⁴ also give high concentrations in the anterior chamber and should be used whenever possible in place of injections into the anterior chamber. Thus, unnecessary trauma to the intraocular structures of the anterior segment will be avoided.

These studies indicate that with increase in capillary permeability, such as occurs in eyes with intraocular inflammation, the penetration of penicillin into the vitreous is greater than the penetration of the substance into the vitreous of the normal eye when locally or systemically administered. The difference between the penetration of penicillin into the vitreous of normal eyes and the penetration into the vitreous of inflamed eyes is less than the difference in the concentration of penicillin reached in the aqueous of normal eyes and the concentration reached in the aqueous of inflamed eyes. The levels of penicillin in the vitreous of eyes with inflammation of the anterior segment following intramuscular administration, as recorded here, are considerably less than the concentrations observed by Leopold and La Motte⁵ in the aqueous humor of eyes with corneal infections. Our observations are similar to those of Duke-Elder,¹³ who stated that the vitreous resembles the aqueous in the quality of its changes in content secondary to alterations in capillary permeability but that the changes in the vitreous are smaller, take longer to reach a maximum and return more slowly to normal than do the changes in the aqueous. It has also been noted by many observers that the increase in capillary permeability is greater in the experimental animal, especially the rabbit, than in man.^{13b} Therefore, although it is important to determine the concentration of penicillin in the

vitreous of inflamed eyes before any method of therapy is recommended, the data reported here indicate that this concentration is not so important a factor in the case of the vitreous humor as in that of the anterior segment of the eye.

It is interesting to note that although high concentrations of penicillin are produced in the anterior chamber, relatively little penicillin reaches the vitreous chamber. This supports the belief that the iris-lens contact is fairly close and that the flow of substances in the anterior chamber is largely away from the vitreous.^{13c} Adler's¹¹ studies with sugar indicated this. In this investigation he suggested that iridectomy might increase the concentration in the vitreous of substances placed in the anterior chamber. In the eyes with small iridectomies penicillin reached the vitreous from the anterior chamber in higher concentrations than it did in normal eyes. This study suggests that corneal iontophoresis or injection of penicillin into the anterior chamber might give adequate concentrations of the substance in the vitreous in eyes with iridectomy, aphakia or partial or complete removal of the lens-iris barrier. Dunnington and von Sallmann¹² reported 3 cases of endophthalmitis, probably due to *Staph aureus*, in aphakic eyes. In these cases penicillin iontophoresis was used, with successful regression of the infection in 1 case, with regression but loss of visual ability in another and with total failure in the third.

It is tempting to speculate on the reason for the failures of subconjunctival injection and injection into the anterior chamber to control successfully experimental infection in all cases reported here, even though these methods produce theoretically adequate concentrations of penicillin in the vitreous of the inflamed eye. It may be that the penicillin diffuses slowly and unequally through the vitreous gel. It is also possible that the organism is not so susceptible to penicillin in the vitreous gel as in serum or aqueous humor. It may be that the infection was too overwhelming. However, it is important to note that these methods were partially successful in controlling the infection in 4 out of 10 eyes. One may conclude that methods of producing high concentrations of penicillin in the anterior chamber, such as iontophoresis² and injections into the anterior chamber, as well as subconjunctival injections,⁴ have merit in treating ectogenous infections of the vitreous due to a penicillin-sensitive organism. In the presence of a break in the lens-iris barrier, such methods may be more successful. However, no one of these methods

12 Dunnington, J. H., and von Sallmann, L. Penicillin Therapy in Ophthalmology, *Arch Ophth* **32** 353 (Nov) 1944

13 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St Louis, C. V. Mosby Company, 1939, vol 1, (a) p 466, (b) p 441, (c) p 468

14 Adler, F. H. Sugar Content of Ocular Fluids, *Tr Am Ophth Soc* **28** 307, 1930

is as efficient as intravitreal injections of penicillin

SUMMARY

1 Intramuscularly and intravenously administered penicillin in a concentration of 4,000 units per kilogram failed to produce detectable concentrations of penicillin in the vitreous humor in the normal rabbit eye

2 Prolonging the length of time that penicillin remained in the blood stream by employing a penicillin-gelatin-vasoconstrictor preparation failed to increase the intravitreous penetration of penicillin from the blood stream in the normal rabbit eye

3 Subconjunctival injection of penicillin and injection of the substance into the anterior chamber produced detectable concentrations of penicillin in the vitreous in the normal rabbit eye

4 All methods of administration produced higher concentrations of penicillin in the vitreous humor in the rabbit eyes with infection of the anterior chamber than in normal eyes

5 Theoretically adequate concentrations of penicillin in the vitreous were obtained with administration of penicillin by subconjunctival

injection and by injection into the anterior chamber in the inflamed rabbit eye. Such levels were adequately maintained for three hours after one injection

6 Higher concentrations of penicillin in the vitreous were obtained in eyes with iridectomies than in normal eyes after injections of penicillin into the anterior chamber

7 Intravenously administered penicillin failed to stop the progression of experimentally induced ectogenous infections of a vitreous caused by a penicillin-sensitive strain of *Staph aureus*

8 Repeated subconjunctival injections of penicillin and injections into the anterior chamber halted the progress of intravitreal infection due to *Staph aureus* in 4 of 10 rabbit eyes

9 Intravitreal injections halted the progress of ectogenous infections of the vitreous due to *Staph aureus* in all eyes receiving one injection consisting of more than 500 Oxford units of penicillin. Lower concentrations than this, including 5 units per injection, were partially successful

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CYCLOPIA COMPLETA AND ARHINENCEPHALIA COMPLETA WITH UMBILICAL HERNIA IN A FULL TERM CHILD

REPORT OF A CASE

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Recently there came into my hands the case history and excellent photographs of a human monster at term with cyclopia completa, arhinencephalia completa and umbilical hernia. The materials were brought to me by Mr Daniel B Levy, a student in the University of Virginia Medical School, who obtained them through the courtesy of Dr H M Digges, of Suffolk, Va., the attending physician. The specimen is of special interest because it was one of those extremely rare monsters in which there is absolutely no trace of a nose and yet aside from this defect and the presence of the cyclopean eye the face shows only a slight degree of abnormality.

Hannover (1882) collected the reports of 103 cases of cyclopia in man which had been published up to that time¹. Examination of the reference to cyclopia in man in the *Quarterly Cumulative Index Medicus* and in the "Index Catalogue of the Library of the Surgeon-General's Office of the United States Army" since that time has revealed 92 instances reported since 1882. This total of 195 cases is a rather low incidence of malformation compared with the incidence of malformation in other parts of the body. Thirty of these cases in which the anomalous conditions are well discussed and illustrated and which seem to be representative of the variations which accompany cyclopia have been used as a background in describing the present specimen.

HISTORY OF THE CASE

The father was 28 years of age, the mother, aged 25, had previously borne 2 normal living children. Both parents were Negroes. Wassermann tests gave negative reactions. Both parents said they had not had any venereal disease. The mother suffered severe suprapubic pain during the last three months of pregnancy. There was no evidence of toxemia before, during or after delivery. The recovery was normal. Labor began at term and lasted from 10 a.m. to 10 p.m. The child was born in the left occipitoanterior position.

The child, who was thought to be female, weighed 10 pounds 2½ ounces (5,775 Gm). There was four or five times the usual amount of amniotic fluid. The only signs of life were a few muscular movements,

which subsided practically at once. There was no evidence that the lungs were ever expanded. The body was covered with a persisting lanugo, and the hair on the head was excessively long. There was no nose. A single eye was present in the center of the face. The eye was open at birth and remained so. A mouth was present. The limbs and feet were symmetric and of normal shape, but rather short and stubby. There was a large umbilical cord, into the base of which there was a definite umbilical hernia, with viscera protruding into the sac. Necropsy was not permitted.

DESCRIPTION OF THE SPECIMEN AND COMMENT

The statements just given were made by Dr. Digges. Although a necropsy was not performed and the internal anatomy could therefore not be examined, the unusual nature of the specimen seems to warrant recording. The pictures shown in the text were taken immediately after birth and are clear enough to permit amplification and interpretation of the facts supplied by Dr. Digges.

A photograph of the whole body is shown in figure 1. The child is large—probably the largest on record with a cyclopean eye. In 16 cases of cyclopia in which the weight at birth of the specimen was given, the range was from 1,075 to 3,750 Gm (average weight 2,000 Gm). Most of the cyclopean monsters have been premature babies of the seventh or eighth month.

In 17 cases in which observations were made of the viability of the child at birth 9 babies were stillborn, of whom 4 were viable up to the time of birth and 2 lived for fifteen minutes, 2 for one-half hour and 4 for one hour, two hours, three hours and four hours respectively. It is generally agreed that there is no reliable record of survival of a human cyclopean monster for any great length of time. Hence the paucity of signs of life exhibited by this specimen is not unusual.

The presence of a greater amount of amniotic fluid than is normal suggests that hydramnios was present. Such a condition is not unusual in human cyclopia, since in 16 cases from the modern literature in which histories of the conditions at birth were given hydramnios was present in

1 Hannover, A., cited by Adelmann²⁴.

6 cases, or 37 per cent. Such an incidence of hydramnios is significantly greater than in single births from unselected populations, where it has been estimated to be about 0.5 to 1.0 per cent.² The etiologic significance of hydramnios in relation to cyclopia has not been explained, but it might be suggested that hydramnios is an expression of general physiologic disturbance in the environment in which the embryo has developed.³ This state of the environment may also be related to the age and condition of parity in the mother, since in 15 cases for which the latter information was given no mother was younger than 27 years and there were only 2 primiparas.



Fig 1.—The cyclopean monster as viewed from the right side to show the size and position of the umbilical hernia (Photograph by Gerald Rose.)

The proportions of the body of the monster are in general normal, but there is a tendency toward shortness of limbs and digits. The umbilical hernia is the most striking abnormality of the body aside from those of the face. The position, size and shape of the hernial sac are well shown in figure 1. The viscera protrude into a translucent membranous sac at the base of the umbilical cord. This sac consists

² Szendi, B. Ueber die Bedeutung der Struktur der Eihäute und des Gefassnetzes der Placenta auf Grund von 112 Zwillingengeburten, *Arch f Gynak* **167** 108 (May) 1938.

³ Mall, F. P. A Study of the Causes Underlying the Origin of Human Monsters, *J Morphol* **19** 3 (Feb) 1908.

of the amnion fused with a remnant of the original wall of the embryophore. The nipple-like structure at the right of the mass is a small piece of protruding intestine. This malformation has been reported in human cyclopean monsters, according to Chidester⁴ and Ognew,⁵ but I have found no reference to it in the modern literature. Ognew interpreted umbilical hernia and other malformations which have been reported to accompany cyclopia as evidence for the centrifugal spreading of biologic agents of destruction. He expressed the opinion that malformations may be attributed to developmental disturbance of the formative cells from which the embryo differentiates. The greatest modifications of development take place in a weak central region, such as the cephalic end of the body, and from there may spread peripherally and not only radically alter normal development but affect detrimentally cells or organs which hitherto have been completely normal.

The external genitalia in this specimen do not appear to be normal. From the immediate examination Dr. Digges thought they were female, but if this is the case the condition apparent in the photograph indicates that the clitoris is larger than normal. The alternative is incomplete development of the labioscrotal swellings and hypopspadias, conditions which cannot be decided by examination of the picture. Abnormalities of the external genitalia, particularly in female cyclopeans, have been reported, but in descriptions of 30 representative cyclopeans there are only 2 references to malformed genitalia, and in both of these specimens the organs were undeveloped male organs.⁶

The excellent photograph of the face as viewed from the front (fig 2) allows a more detailed examination of the features. The head is set squarely on the shoulders, and there is little if any neck. The back of the head is much broader than the face and can be seen bulging behind the ears. In 8 of the representative 30 specimens to which I referred the head was so set on the shoulders. In the present specimen the whole top and back of the head are covered with long black hair, which extends down on the front of the head almost to the eye. Specific mention of long hair extending down on the

⁴ Chidester, F. E. The Origin of Cyclopean Monsters, *Am Nat* **57** 496 (Nov-Dec) 1923.

⁵ Ognew, B. W. Die Cyclopie im Zusammenhang mit Anomalien anderer Organe, *Anat Anz* **70** 241 (Sept) 1929.

⁶ (a) Burns, W. Cyclopean Monstrosity, Boston M & S J **68** 513 (July 30) 1863. (b) Chapman, K. H. Human Cyclopia, *Arch Ophth* **16** 40 (July) 1936.

forehead has been made in several descriptions,⁷ and in practically all of the pictures from the most recent literature the hair seems to be more profuse than in normal newborn children.

There is practically no forehead, a characteristic common to most cyclopeans. On the margins of the space immediately above the eye are the rudiments of eyebrows or superciliary ridges, which are separated from each other in the middle line and which extend over the lateral margins of the eye at an angle of about 45 de-



Fig 2.—A front view of the face of the cyclopean monster (Photograph by Gerald Rose)

grees. These partial eyebrows are covered with long hairs which extend laterocephalad at right angles to the direction of the ridges. The point at which each eyebrow ends medially seems to be at the region of the supraorbital notch. Such partial eyebrows in cyclopeans have been recorded by several investigators.⁸ In a normal embryo

7 (a) Allan, R. A Human Astaticous Cyclops, *Lancet* **1** 227 (Feb 26) 1848 (b) Hall, A D. Case of Cyclopic Malformation, *Boston M & S J* **65** 263 (Oct 24) 1862 (c) Smith, S., and Boulgakow, B. A Case of Cyclopia, *J Anat* **61** 105 (Oct) 1926

8 (a) Hall^{7b} (b) Smith and Boulgakow^{7c} (c) Allen, F H. Cyclopia, *M Rec* **50** 249 (Aug 15) 1896 (d) Dougal, D., and Bride, T M. A Case of Cyclopia, *Brit M J* **2** 13 (July 4) 1914 (e) Best, E

of 16 mm the lower lid on each side is already formed as a shelflike process of the maxillary process below the eyeball. Medially it meets the lateral nasal process in the naso-optic groove. The upper lid and the eyebrows start at this time, each as a lateral fold of mesoderm covered with ectoderm which grows first laterally from the supraoptic region and forms the outer canthus.⁹ At the 18 mm stage a new fold appears medial to this and joins the lateral fold to complete the median part of the upper lid and the eyebrow. From such a normal condition it could be inferred that the cyclops lacked not only the primordium of a nose but also that part of the mesoderm which forms the median parts of the eyebrows and the upper lids. The lateral parts did develop, and hence the rudiments of eyebrows. There is the possibility that the lateral parts of the eyebrows and the upper lids are proliferated from the mesoderm of the laterocephalic margin of the maxillary processes, which are undergoing rapid extension at the time the eyelids are forming.

Below the superciliary ridges and the limited central region of the forehead there is a single superior palpebra arching over the open palpebral fissure. This eyelid has no trace of a tarsal arch, and the palpebral fold ends abruptly at the outer canthus, where its lateral margins are overlapped from below by the inferior palpebra. There are suggestions of cilia on the margins, but they are not marked. The inferior palpebrae are only slightly arched, and the two lateral components meet medially at a notch. Each side of the notch meets the lid at an angle characteristic of the normal inner canthus. No puncta lacrimalia can be seen, and there seems to be no trace of cilia, but the lateral ends of the inferior palpebrae appear to have each a tarsal arch.

Of 25 representative specimens of cyclopia, 14 had a single arch formed by the superior palpebra similar to that just described, although not always with the same degree of arching.¹⁰

Zur Frage der Cyclopie und Arhinecephalie, *Beitr z path Anat u z allg Path* **67** 437, 1920 (f) Hagens, E W. Unilateral Malformation of the Ear Associated with Cyclopia, *Arch Otolaryng* **18** 332 (Sept) 1933 (g) Breckwoldt, H. Ueber die Zahnverhaltnisse bei Zyklopie und Gesichtsspaltes, *Beitr z path Anat u z allg Path* **98** 115 (Dec) 1936

9 Mann, I C. *The Development of the Human Eye*, London, Cambridge University Press, 1928

10 (a) Burns^{6a} (b) Chapman,^{6b} case 3 (c) Allan⁷ⁱ (d) Smith and Boulgakow^{7c} (e) Dougal and Bride^{8d} (f) Best^{8e} (g) Hagens^{8f} (h) Scott, J. A Monoculous Male Foetus, *Lancet* **1** 633 (June 14) 1862 (i) Koogler, M A. A Report of Three Human Mon-

Such a morphologic relation is the result of the failure of the median primordia of the upper lids to form. In 9 specimens these primordia had formed, and the upper lid was composed of two parts which met at a notch in the middle line.¹¹ In 2 specimens in which only a rudimentary eye was present the palpebral fissure was a mere slit.¹²

There was only a single specimen in this group with an eyeball in which the inferior palpebrae were undivided.^{10b} In 22 specimens the inferior palpebrae met in a median notch or the lid was divided into halves, which met at an orally directed angle in the middle line.¹³ A common caruncula within the notch between the lower lids, such as is seen in the present specimen, has been described in several other cyclopeans but is not of common occurrence.¹⁴ In 2 specimens puncta lacrimalia were present.¹⁵ The presence of two lower lids notched in the median line but with a single caruncula indicates median fusion of this part of the maxillary processes, since the lower lids are derived from the maxillary processes¹⁶ and the caruncula takes its origin from the primordium of the internal portion of

the lower lid.¹⁷ The caruncula in the present specimen is represented by a single median mass, and since in normal development there is one caruncula for each internal canthus, it would appear that the median fusion is an upward continuation of the fusion of the maxillary processes without intervention of the field formed by the lower border of the frontal process.

Within the widely open palpebral fissure can be seen the external surface of what appears to be a single eyeball supported in a single orbit. There is a distinct transparent cornea, which is circular in outline. Within this can be seen the outline of an iris, in the middle of which is a definite circular pupil. The bright appearance of the pupil in the photograph would imply that there is an opaque membrane behind this region, otherwise the pigment of the interior would give the pupil a dark color.

The anatomy of the eyeball in human cyclopeans has been examined by many investigators, and all degrees of separation, from a single optic globe to double globes lying within a common orbit, have been described. Thus of 29 reports examined the eyeball was described as single in 13.¹⁸ In 2 specimens the eyeball looked single from the outside, but the globes were separate internally.^{10l, m} There was complete duplication in a single orbit with a common palpebral fissure in 10 specimens.¹⁹ There were 4 instances of arrest in development of the optic globe such that the region of the eye was represented by a rudimentary sac.²⁰ These conditions represent the typical malformations of the eyeball in cyclopia that can be seen in general from the outside. The specimen described here apparently belongs in the class with a single undivided eyeball in a single orbit, although a categorical assertion that this is true cannot be made because necropsy

strosities, Am J M Sc **84** 129 (July) 1882 (j) Falk, J C A Specimen of Cyclocephalus, Philadelphia M J **4** 671 (Oct 7) 1899 (k) Wilder, H H The Morphology of Cosmobia, Am J Anat **8** 355 (Dec) 1908 (l) Jackson, H Cyclopean Monster, J A M A **53** 1483 (Oct 30) 1909 (m) Humphrey, R R A Case of Cyclopia in Homo, Anat Rec **28** 207 (Aug) 1924 (n) Wilber, I E Human Cyclopia Associated with Other Ocular Anomalies, Am J Ophth **22** 1120 (Oct) 1939

11 (a) Chapman,^{6b} cases 1 and 2 (b) Allen^{sc} (c) Breckwoldt^{sg} (d) Jackson, H Cyclopean Monster, Tr Chicago Path Soc **9** 71, 1913 (e) Der Brucke, M G Cyclopia, Arch Ophth **15** 114 (Jan) 1936 (f) Kuperstein, D Cyclops Case, Am J Surg **33** 148 (July) 1936 (g) De, M N, and Dutta, H K A Case of Foetus with One Eye (Cyclops), J Anat **73** 499 (April) 1939

12 (a) Galloupe, I F Combination of Cyclopia and Anterior Hydrencephalocoele, Boston M & S J **102** 495 (May 20) 1880 (b) Durlacher Zur Kasuistik der Zyclopie mit Russelbildung, Deutsche med Wchnschr **41** 1128 (Sept 16) 1915

13 (a) Ognew⁵ (b) Chapman,^{6b} cases 1 and 2 (c) Allan^{ra} (d) Smith and Boulgakow^{rc} (e) Allen^{sc} (f) Dougal and Bride^{sd} (g) Best^{se} (h) Hagens^{sf} (i) Breckwoldt^{sg} (j) Scott^{10h} (k) Koogler¹⁰ⁱ (l) Falk^{10j} (m) Wilder^{10k} (n) Jackson^{10l} (o) Humphrey^{10m} (p) Wilber¹⁰ⁿ (q) Francis, D J T A Short Account of a One-Eyed Monster, London M Gaz **34** 580 (Aug) 1844 (r) Jackson^{11d} (s) Der Brucke^{11e} (t) Kuperstein^{11f} (u) De and Dutta^{11g}

14 Smith and Boulgakow^{rc} Allen^{sc} Falk^{10j} Wilder^{10k} Humphrey^{10m}

15 Dougal and Bride^{sd}, Wilder^{10k}

16 Kollman, J Entwicklungsgeschichte des Menschen, ed 1, Jena G Fischer, 1898

17 Ask, F Ueber die Entwicklung der Caruncula lacrimalis beim Menschen, Anat Anz **30** 197 (March) 1907

18 Burns^{ea} Allan^{ra} Smith and Boulgakow^{rc} Allen^{sc} Breckwoldt^{sg} Scott^{10h} Koogler¹⁰ⁱ Falk^{10j} Francis^{13q} Der Brucke^{11e} Kuperstein^{11f} De and Dutta^{11g} Bingham, A W Full Term Cyclops, Am J Obst **77** 150 (Feb) 1918

19 (a) Ognew⁵ (b) Chapman,^{6b} cases 1 and 2 (c) Dougal and Bride^{sd} (d) Best^{se} (e) Hagens^{sf} (f) Wilder^{10k} (g) Wilber¹⁰ⁿ (h) Jackson^{11d} (i) von Monakow, C Cyklopie mit Verdopplung des Rückenmarken, Wien med Wchnschr **46** 2222 (Dec 12) 1896

20 (a) Hall^{rb} (b) Galloupe^{12a} (c) Durlacher^{12b} (d) Rothschild, P Arhinencephalia completa Eine neue Form der Arhinencephalie mit Betrachtung über die formale und kausale Genese von Arhinencephalie und Cyklopie, Beitr z path Anat u z allg Path **73** 65 (Jan) 1924

was not permitted. The underlying causes of these variations will be considered.

A nose is absent. There is no trace of any organ which could resemble a nose. It is well known that when cyclopia occurs in man there is usually a cylindric or piriform proboscis above the single median eye. This may be a simple saclike organ, or in its walls there may be cartilage or even osseous tissue. It is usually pierced at the distal end by a small opening. In 19 of 29 cases which may be taken as representative of conditions of nasal development which have been found in human cyclopean monsters, a proboscis lying immediately above the eye was described. In 16 of these in which the length of the proboscis was given the range was from 10 to 37 mm (average, 23 mm), in 13 cases in which the diameter was given the range was from 8 to 20 mm (average, 13 mm). Thus it would seem that when an effort at formation of a nose is aborted by the failure of the primordia of the eye to divide there is a degree of regulation of form in the product of this attempt, otherwise the range in size, shape and position of the abortive structure would be considerably greater.

In 1 specimen there was a proboscis below the single eye²¹ but a mouth was lacking, and the condition suggests that this was an abortive attempt to form a mouth from reduced maxillary processes and that it cannot be interpreted as an aborted nose.

In 8 cyclopeans there was no trace of a nose, in 4 which were similar to the specimen here described there was nothing on the forehead above the eye²². In 2 specimens the forehead was obliterated by a fluid-filled meningocele²³. In 1 there was a puffy swelling above the eye,^{10h} and in another there was a cartilaginous rudiment above the eye¹⁰ⁱ.

Accordingly, the condition here described is an example of a rare type of arhinencephalia completa accompanying cyclopia completa in which the primordia of the nasal organ have been completely suppressed or have failed to be induced during development. The picture of the present specimen shows this condition to better advantage than any other published pictures.

Below the eye in the normal place for the nose there is a wide stretch of skin where the cheeks are continuous with each other. Such a wide space was present in 18 of 29 specimens whose faces have been described. On the upper

margin of this region and just below the eye there is a furrow which marks the lower border of a slight swelling. This line is interpreted to be the result of the fusion of the two suborbital furrows, which in the normal binocular condition are present below the eyes²³. This feature is present and well marked in 5 of the 29 cyclopeans²⁴. Below this furrow and separated from it by a narrow isthmus of skin is a deeper groove extending across the face. This groove is interpreted as having been formed by the confluence of the nasolabial furrows, which in the normal fetus extend from the margins of the nose to the lateral borders of the lips and which in the absence of the nose and by the medial fusion of the maxillary processes extend across the face. This feature was present in the same region in 3 specimens²⁵. The space between the two furrows is interpreted as an external expression of a medial fusion of the buccal fat pads. Below the nasolabial groove the upper lip begins to protrude, and this protrusion extends down to the margin of the upper lip. The swelling fades laterally into the regions of the cheeks.

The mouth in the present specimen is complete, but the upper lip lacks a philtrum and a labial tubercle. Such a condition is characteristic of the mouth in human cyclopeans. The philtrum and the labial tubercle are lacking because the median nasal processes were never formed. There is no trace of the fusion which must have taken place between the maxillary processes to complete the upper border of the mouth. Close examination of the mouth shows that there is a large central process which extends downward from the upper lip and meets the broad shelflike lower lip. The lower lip projects in normal fashion and is separated from the chin by the usual sublabial furrow. This condition was present in 17 specimens out of 25 described. In contrast, there were 2 specimens, both synotic, in which the mouth was absent and the ears were in the region of the lateral margins of the chin²⁶. A median cleft lip, in which the medial margins of the maxillary processes had failed to fuse, was present in 3 specimens²⁷. In 2 specimens the mouth was a rudimentary sac with no

23 Smith, R. M., and Parker, A. J. Dissection of a Human Otocephalic Cyclops Monstrosity, Am. J. M. Sc. 84: 132 (July) 1882.

24 Smith^{2e}, Dougal and Bride^{8d}, Wilder^{10k}, Der Brucke^{11e}, De and Dutta^{11g}.

25 Dougal and Bride^{8d}, Der Brucke^{11e}, De and Dutta^{11g}.

26 Allan^{7a}, Francis^{13q}.

27 Hagens^{8f}, Scott^{10h}, Rothschild^{20d}.

21 Smith and Boulgakow^{7c}, Hagens^{8f}, Breckwoldt^{9g}, Humphrey^{10m}.

22 Francis^{13q}, Galloupe^{12a}.

inferior maxillary region²⁸ Microstomia was present in 1 cyclopean²⁹

From the summary just given of the varying conditions of the mouth in human cyclopeans it can be seen that all degrees of development of the maxillary processes of the first branchial arch occur. These variations also indicate that formation of the upper lip without the median nasal processes is possible and that the maxillary processes have potential powers of growth which are usually limited by the presence of the median and lateral nasal processes. Defective development is an indication of an inherent condition of weakness of the primordia or is the result of the action of external agents on the fundamental primordia at the time when form should be regulated,³⁰ but the extent of weakness or of biologic deficiency is variable. Thus, in those cases of cyclopia in which the upper lip is not cleft there is relatively little deficiency in the capacity of the parts below the eye to develop along normal lines, but when the lip is cleft or the mouth deficient there is evidence of a greater degree of developmental weakness. Since the molding of these parts is in large measure determined by regulation of the mesoderm,³¹ the modern conception is that defective distribution or faulty migration of mesoderm explains not only the failure of the primordia of the eye to divide as they should but also the defective molding of other features of the face.

The auricles of the external ears in this specimen are far down on the sides of the head, and the lower border of the left ear rests on the shoulder. In both ears the dorsal part of the helix, the part contributed by the tissue immediately above the first branchial arch, is lacking. Also, the cephalic part, contributed by the cephalic margins of the cleft, are thicker than normal, giving the ear a "cauliflower" appearance. Malformation of the ears is an unusual accompaniment of cyclopia. Of 28 cyclopeans whose ears were mentioned there was none in whom both ears were absent. In 1 specimen the left ear was absent and the right was normal,³² and in 1 the external ears were underdeveloped.³³ There were 2 specimens with synotica.³⁴ In 1 specimen the ears were well down on the neck and were larger than normal.³⁵ In only 1^{2d}

cyclopean were the parts deficient in the same regions and folded in the same manner as in the specimen described here. In 1 specimen the ears were abnormally large.^{10m} In the remaining 21 there was nothing unusual about the external ears.

EARLY EMBRYONIC RELATIONS OF OPTIC PRIMORDIA

To attempt an explanation of the factors in early human development which underlie the production of cyclopia, one must understand the relations of those parts of the embryo which precede the actual morphologic appearance of the optic primordia. The earliest appearance of the optic primordia which can be morphologically identified was stated by Bartelmez and Evans³² to be present in a young human embryo of 8 somites (H87, University of Chicago collection). These primordia are two grooves, the optic sulci, which, arising in the laterodorsal part of the primordium of the forebrain, extend obliquely mesiad and terminate in a thickened medial plate which is unpaired, the so-called torus opticus. Prior to this time the neural plate, such as is present in the Ingalls embryo of 2 somites,³³ shows the primordium of the plate of the forebrain with a suggestion of the optic sulci. The crucial stage at which cyclopia may be initiated must occur before this stage of development. This conception is held by those investigators who have examined by experimental methods the morphologic conditions incident to the production of cyclopia in amphibia. These experiments were reviewed in detail by Adelmann,³⁴ and an analysis of the data indicated that chemical and physical agents acting on embryos prior to the appearance of the primordia of the eye cause cyclopia. Also, experiments in extirpation and transplantation have shown that the whole region of the forebrain prior to the appearance of bilateral optic primordia is capable of forming eyes from any region, but that the formation is best from median pieces. Hence the idea has arisen that the optic primordia are gradually localized laterally under the influence of some agent of induction which modifies the primitive general potency for production of the eyes. The part which Adelmann³⁰ considered to be the causa-

28 (a) Smith and Boulgakov^{2e} (b) Koogler¹⁰
The same case is described by Smith and Parker²³

29 Holtfreter J Formative Reize in der Embryonalentwicklung der Amphibien, dargestellt an Explantationsversuchen, Arch f exper Zellforsch **15** 281, 1934, cited by Adelmann³⁴

30 Adelmann, H B A Study of Cyclopia in Ambystoma Punctatum with Special Reference to the Mesoderm, J Exper Zool **67** 217 (Feb) 1934

31 Koogler^{2b} Francis^{13q}

32 Bartelmez, G W, and Evans, H M Development of the Human Embryo During the Period of Somite Formation, Including Embryos with 2 to 16 Pairs of Somites, Contrib Embryol **17** 1 (Feb) 1926

33 Ingalls, N W A Human Embryo at the Beginning of Segmentation with Special Reference to the Vascular System, Contrib Embryol **11** 61 (Jan) 1920

34 Adelmann, H B The Problem of Cyclopia I, Quart Rev Biol **2** 161 (June) 1936, II, ibid **2** 284 (Sept) 1936

tive agent in this bilateral induction is the prechordal plate, a mass of tissue (mesentoderm) lying in the roof of the most cephalic part of the archenteron at the stage immediately preceding the appearance of bilateral optic primordia. In experimental procedures in which cyclopia has occurred after the exposure of amphibian embryos to lithium salts, the prechordal plate, which normally flattens and progresses laterally, does not do so. Whether this relation between failure of the prechordal plate to produce bilateral formation of the eyes is mechanical or chemical has not been decided.

Similar conditions of development in human embryos before the morphologic appearance of primordia of the eye can be found in the Mc-Intyre embryo,³⁵ in which there was a rather extensive prochordal plate (the morphologic antecedent of the prechordal plate) underlying the cephalic part of the early neural plate. And in the embryos of still younger stages described by Heuser³⁶ and George³⁷ the prochordal plate lay in the roof of the archenteron but no neural plate was present as yet in this part of the embryonic disk. Hence if inhibition of or interference with the growth of the neural plate to form bilateral primordia of the eyes is to occur it must take place between the stages represented by the embryos of Heuser and George and the stage described by Ingalls or that of Bartelmez and Evans.

Unfortunately the interval of time between these stages in human embryos is not definitely known. Time seems to me an important factor to consider if information gained from experiments with animals is to be applied to human development. Not only are human beings different from animals in certain morphologic and physical aspects, but the time relation of the changes in their tissues to their environment is different. In the preceding paragraph it was pointed out that the morphologic conditions preceding development of the eye in human beings are similar in a general way to those in amphibia, but the element of time is different. We know from the measurements of these periods in the lower vertebrates that a certain interval of time elapses between the first appearance of the neural plate and the morphologic appearance of the primordia of the eye. I have estimated this

interval as follows from the data in published tables of early development in certain vertebrates in the embryo of the frog, for *Rana sylvatica* four hours³⁸ and for *Rana pipiens* twelve hours³⁹, in the embryo of the salamander for *Triturus pyrrhogaster* twelve hours⁴⁰ and for *Ambystoma punctatum* six hours⁴¹, in the embryo of the chick four hours⁴², in the embryo of the guinea pig twenty-four hours⁴³, in the embryo of the rabbit seven hours,⁴⁴ and in that of the macaque monkey two days.⁴⁵ Examination of these data shows that the greatest interval of time between these two stages occurs in the growth of the monkey embryo. If it is assumed that there is little difference between monkeys and human beings as regards the time of appearance of certain structures it may be concluded that these changes occur in human beings between the nineteenth and twenty-first day of development. Hence if certain environmental conditions can affect the neural plate so that the formation of bilateral primordia of the eye is inhibited the time during which these detrimental influences may act is considerably longer in human beings than in the lower vertebrates. The failure of the neural plate to undergo proper morphologic changes also involves changes which could affect the bilaterality of the whole cephalic end of the head, including the forehead, the nasal organs and the brain.⁴⁶ The degrees of cyclopia which are accompanied by varied morphology of other parts of the head can therefore be related to time as well as to early morphologic relations. In the present specimen the modifications have affected the eye, the forehead and the nasal primordia, but no information is available concerning the brain, although from the descriptions of cyclopeans referred to in the preceding pages it would appear that the cerebral part of the brain is usually deficient.

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DEVELOPMENT OF GALACTOSE CATARACT IN THE ALBINO RAT EMBRYO

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In 1935 Mitchell¹ first reported the type of cataract in rats which results from a diet containing a high level of galactose. Subsequent investigation² brought out the fact that galactose cataract occurred more readily in younger than in older animals, and consequently it became of interest to determine the effect of galactose on the developing lens of the rat embryo. A series of investigations, begun in 1937, have definitely established the fact that when pregnant female rats are fed a diet containing 25 per cent galactose cataractic changes appear in the lenses of the embryos.³

Because of variations in the degree of susceptibility of different strains of rats,⁴ the investigation included animals from the original Battle Creek stock, known to be highly susceptible, and from a closely inbred strain which had been used in the Wellesley College laboratory for several years. Preliminary experiments with a lactose diet established the latter strain as somewhat less susceptible. In addition, a hybrid strain was developed by mating males of the Battle Creek strain with females of the Wellesley College strain. Any study of rat embryos brings out the fact that not only do litters vary but individuals within the same litter may show a wide divergence in the stage of development reached within a given time. General conclusions as to the condition at a particular age must be based on a study of a considerable number of individual embryos. Moreover, a knowl-

edge of normal development is essential to the interpretation of abnormal conditions. Therefore, with the three strains of rats, a careful study has been made of more than 300 lenses from a normal series and an approximately equal number from the experimental series.

All of the control animals and all of the females up to the onset of pregnancy were fed a standard ration consisting of Purina dog chow (obtained from the Purina Mills, St. Louis) and lettuce. The original experimental diet was modified according to suggestions made by Dr. Mitchell and was designed to satisfy the increased requirements of pregnancy.⁵ Determination of the age of the embryos was based on the calculations of Long and Evans,⁶ who asserted that fertilization of the eggs might occur at any time within twenty-four hours after copulation. Accordingly, the second day after the appearance of sperm in the vaginal smear was regarded as the first day of gestation, and the rats were 21 days old at the time of birth.

The lens is a particularly difficult organ to prepare for histologic investigation, and it was necessary to try several methods before satisfactory sections could be secured.⁷ The procedure which ultimately gave the greatest detail

5 The composition of the experimental ration was as follows

Corn starch	40%
Galactose	25%
Casein	15%
Hydrogenated cotton seed oil (Crisco)	9%
Wheat germ	5%
F R L salt mixture*	4%
Cod liver oil	2%
Brewers' yeast (given 6 days a week)	0.5 Gm

* Substituted for the Osborne-Mendel salt mixture (F R L salt mixture is described in Hawk, P B, and Bergeim, O. Practical Physiological Chemistry, ed 11, Philadelphia, P Blakiston's Son & Co, 1942, p 887).

6 Long, J A, and Evans, H M. The Oestrus Cycle in the Rat and Its Associated Phenomena, Mem Univ California 6:17, 1922.

7 Dr Theodore L Terry, of the Massachusetts Eye and Ear Infirmary, Boston, gave assistance and suggestions in the initial stages of the investigation.

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4 Mitchell, H S. Susceptibility of Different Strains of Rats to Nutritional Cataract, J Nutrition 12:447, 1936.

of cell structure with the least possible shrinkage and distortion of tissues consisted in preservation in Perényi's fluid, dehydration in alcohol, clearing in cedar oil and embedding in paraffin. It proved difficult to remove the lens without injury and consequent disturbance of the histologic picture. Better results were secured when the lens remained within the eye. However, serial sections were made of both lenses and eyes. These were cut at 10 microns and stained with Delafield's hematoxylin and eosin.

Normal development of the lens showed considerable similarity in all three strains of rats, and the early stages resembled closely the same stages in the rabbit, as described by Rabl.⁸ With increasing differentiation of the lens there appeared greater variation between individual rats, and even between the two eyes of the same animal. Development evidently did not progress uniformly throughout the lens. Certain conditions could be considered characteristic of each age, however.

The placode of the lens appeared as a thickening of ectoderm at the age of 10 days. Invagination and closure of the lens vesicle occurred during the eleventh day, and the vesicle became separated from the overlying ectoderm on the twelfth day. At this time cells in the posterior portion had begun to lengthen, and by the thirteenth day the lumen of the vesicle was almost obliterated by growth of the posterior cells, and there was an obvious distinction between the anterior epithelium and the posterior fibers of the lens. By the fourteenth day the anterior epithelium consisted of a single layer of high cuboidal cells, which became columnar at the equator. Growth of the posterior fibers had been greater in the central region, with consequent forward migration of their nuclei. Sections through the dorsoventral axis at this stage showed the nuclei in a curve following the curve of the anterior surface of the lens. A few lenses at the 14 day stage showed extremely small, single vacuoles either within or between certain of the posterior fibers. These vacuoles were apparently empty and were not numerous. In the 15 day lens the most conspicuous feature was the great increase in vacuoles. They had spread throughout the entire central portion and occupied a region which was roughly V shaped in section, with the angle of the V at the posterior pole of the lens and the broad area immediately below the anterior epithelium. The vacuoles might occur singly or in groups, and certain of them

contained a fine reticulum, which stained pink with eosin. They decreased rapidly in number during the sixteenth day. Those that remained appeared, generally, at the posterior pole of the lens in the region where the fibers were converging to form the posterior suture (fig 1A). This suture showed distinctly at 17 days as a depression in the posterior pole of the lens at the point where the hyaloid artery touched the capsule (fig 1B). In section, the suture was in the form of an inverted V and contained dark-staining granular material, in which were a few vacuoles of varying sizes.

Further differentiation of the lens occurred at 18 days. The anterior epithelium became low cuboidal. The central fibers developed into the nucleus of the lens, a change which involved enlargement of the individual fibers and gradual disappearance of their nuclei. The structure of the cytoplasm altered, some fibers staining more and others less deeply (fig 1C) but all being densely granular. Fibers just peripheral to the lens nucleus showed a fine reticular cytoplasm and appeared pale, in contrast to the fibers of the nucleus itself. All fibers immediately outside the lens nucleus converged toward the posterior suture, which frequently contained more or less dark-staining granular material and vacuoles. By this time vacuoles had entirely disappeared from the main body of the lens. At the anterior pole a few peripheral fibers met above the lens nucleus to form the anterior suture. At 19 and 20 days both the sutures and the lens nucleus became increasingly distinct, as a result of continued growth of the lens. In lenses of the hybrid and Battle Creek strains, closure of the posterior suture was definitely delayed, granular material continued to accumulate in the suture, and one or more large vacuoles were present at its inner tip. In the lens of the full term rat (fig 1D), the anterior epithelium was low. The lens nucleus had increased in size through incorporation of the surrounding fibers. The anterior suture was more distinct. The posterior suture was almost or completely closed. In some cases, it still contained small vacuoles throughout its length or at its inner tip, and in certain lenses a band of small vacuoles extended outward from the suture across the posterior part of the lens.

Lenses from the experimental animals showed no striking deviation from normal through the fifteenth day of gestation. At 16 days, however, cataractous changes began to appear. Again, as in the normal series, individual differences were evident. Some of these could be explained on the basis of differences in the degree of sus-

⁸ Rabl, C. Ueber den Bau und die Entwicklung der Linse, *Ztschr f wissenschaft Zool* 67.1, 1900

ceptibility to the cataractogenic diet. For instance, two entire litters of 18 day fetuses, one from the Wellesley and one from the hybrid strain, showed no obvious variation from normal.

In the initial stage, at 16 days (fig 2A), the entire central portion of the lens was completely vacuolated. Increase in the number of vacuoles and coalescence of some to form large, irregular

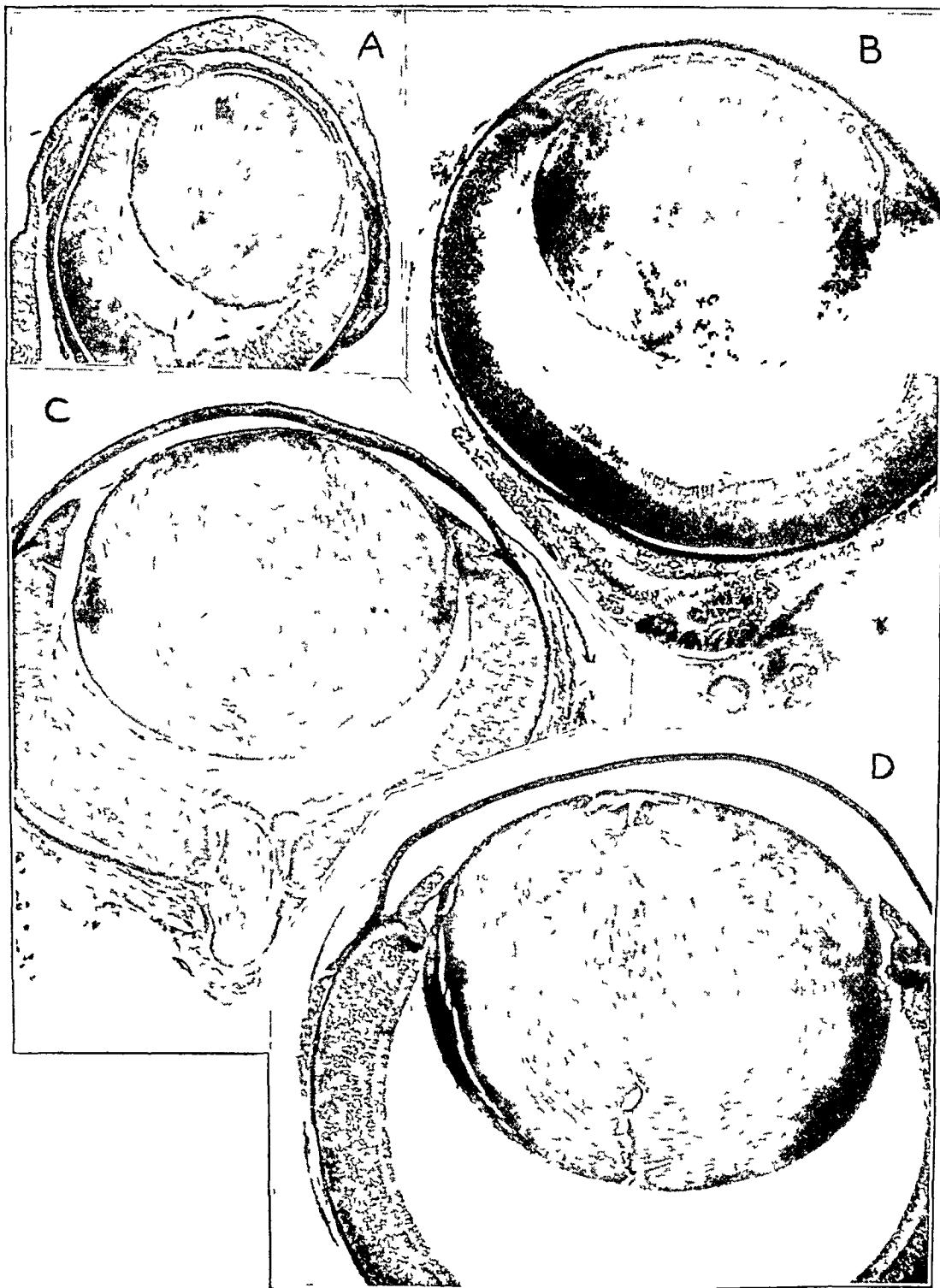


Fig 1 (normal series).—*A*, eye of a 16 day embryo, hybrid strain. *B*, eye of an 18 day fetus, Wellesley College strain. *C*, eye of an 18 day fetus, Wellesley College strain. *D*, eye of a full term rat, Wellesley College strain.

In all the other animals, however, the lenses appeared distinctly abnormal, and the cataractous changes were generally most severe in the Battle Creek strain.

spaces characterized the condition at 17 days (fig 2C). Closure of the posterior suture was slow and permitted greater accumulation of granular material at the posterior pole (fig 2B).

After extensive vacuolation, fibers of the lens nucleus began to lose their structure and were replaced by masses of dense granular material. The degenerative changes appeared first at the

length of the posterior suture. In many cases closure of the suture did not occur, and a wide V-shaped or Y-shaped depression was filled with granular material and vacuoles. Be-

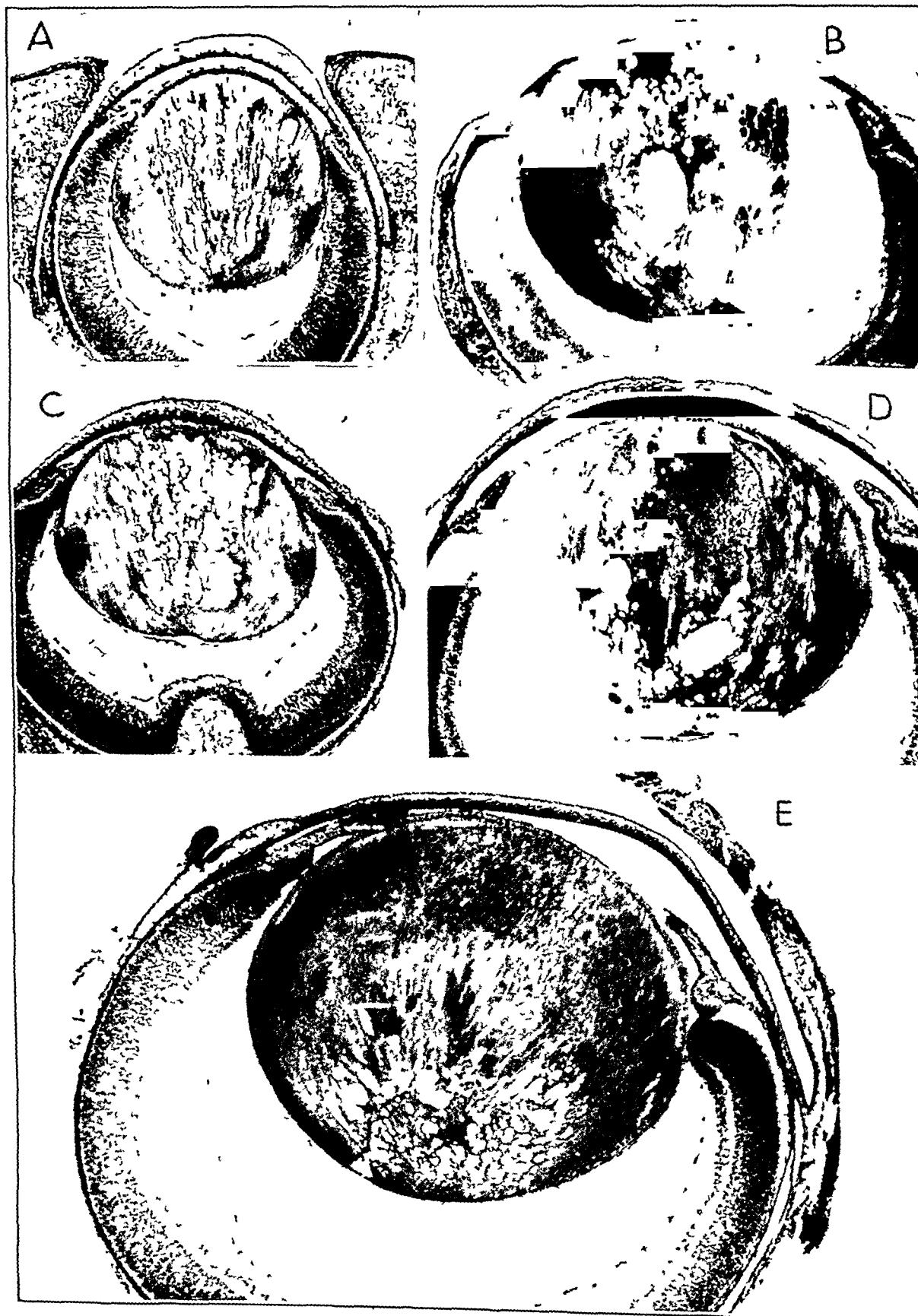


Fig 2 (cataract series)—*A*, eye of a 16 day embryo, hybrid strain; *B*, eye of an 18 day fetus, Battle Creek strain; *C*, eye of a 17 day fetus, hybrid strain; *D*, eye of a 19 day fetus, Wellesley College strain; *E*, eye of a 20 day fetus, Battle Creek strain.

anterior pole of the lens nucleus (fig 2*D*), large, irregular spaces continued to be present at the posterior pole of the lens nucleus. Other smaller, vacuoles extended generally throughout

gaining at 19 days, a band of vacuoles spread peripherally across the posterior part of the lens. These vacuoles radiated from the suture (fig 2*E*) and appeared in many cases to be located

within the fibers themselves. This band increased in extent and was a conspicuous feature of the full term cataractous lens.

Ophthalmoscopic observations on the embryonic lenses were impossible. The histologic changes, however, could be compared directly with those in the lenses of adult rats.⁹ Initial vacuolation was followed by degeneration of fibers and, ultimately, replacement of fibers by a granular mass of noncellular material. Splitting of the suture lines by the accumulation of fluid is also characteristic of this type of cataract.¹⁰ Minute vacuoles beneath the anterior epithelium were observed, but not with sufficient regularity to warrant their inclusion among the specific cataractous changes. There was no apparent modification of either the anterior epithelium or the lens capsule, and any separation of the epithelium from the lens fibers could be regarded only as an artefact, the result of the histologic methods employed. Presence of granular material between the epithelium and the fibers indicated mechanical injury to the lens, inasmuch as it occurred only in lenses which had been removed from the eyes and had suffered distortion or fracture during the operation. While it is evident, therefore, that development of cataract in the embryonic lens is comparable to that in the adult, there are nevertheless obvious differences.

⁹ Gifford, S. R., and Bellows, J. Histologic Changes in the Lens Produced by Galactose, *Arch Ophth* **21** 346 (Feb.) 1939. Dodge, W. M. Jr. Histopathologic Characteristics of Nutritional Cataract in the White Rat, *ibid* **14** 922 (Dec.) 1935.

¹⁰ Yudkin, A. M. Diet and Vitamins in Relation to Cataract, *Am J Ophth* **21** 871 1938.

The location of the primary area of degeneration within the lens nucleus is a characteristic of cataract in the young. Yudkin and Arnold¹¹ found that in young rats the initial opacity occurred in the nucleus, whereas in older rats a cortical cataract developed. If cataract is the result of a metabolic disturbance, presumably those areas of the lens which have a higher metabolic rate should be the most susceptible. The sequence of cataractous changes in the embryo is clearly related to developmental changes within the lens. Onset of the cataract affects the central fibers, which are undergoing modifications preparatory to the formation of the lens nucleus. As development progresses, closure of the posterior suture marks another region of cellular activity, and cataractous changes shift from the central to the more posterior region of the lens. Sections of normal lenses show that vacuoles arise apparently as the accompaniment of normal activity. The extreme vacuolation seems to be due to continuation and exaggeration of a condition which already exists within the lens. Comparison of the photomicrographs, which were all taken at the same magnification, makes it apparent that presence of the cataract does not interfere with normal increase in size of the lens. Thus, it is not the growing regions which are affected but those portions of the lens which are undergoing differentiation.

The photomicrographs were taken by Mr. R. W. St. Clair of Cambridge, Mass.

¹¹ Yudkin, A. M., and Arnold, C. H. Cataracts Produced in Albino Rats on a Ration Containing a High Proportion of Lactose and Galactose, *Arch Ophth* **14** 960 (Dec.) 1935.

FREQUENCY AND LOCATION OF PUNCTATE OPACITIES IN THREE HUNDRED YOUNG CRYSTALLINE LENSES

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The frequency of opacities in the young crystalline lens is so great that it has been considered physiologic by some ophthalmologists. Pellaton,¹ examining 82 children in Basel, Switzerland, found punctiform opacities in 96 per cent of them. Vogt² wrote that in a somewhat older group peripheral hooklike opacities were present in 10 per cent, embryonal axial opacities in the region of the anterior embryonal sutures in 20 per cent and various forms of punctate opacities in the region of the posterior Y sutures in 10 per cent. He stated that the number of punctate opacities increases with age and in the fifth and sixth decade hardly a lens is free of such opacities. This statement recalls the famous dictum of Walther³ that every one who does not die prematurely becomes cataractous.

The purpose of the investigation herein reported was to determine the incidence of opacities in Americans between 18 and 40 years of age and to correlate changes and age in the hope that light might be thrown on the causation of senile cataract. The slit lamp examinations, which were conducted in a United States Army general hospital, were made while the eyes were under homatropine cycloplegia. Altogether 150 subjects, or a total of 300 eyes, were examined. Eyes showing signs of ocular disease or of trauma were excluded.

According to the site in the lens in which they were located, the opacities were classified into the following groups:

- A Those between the anterior band of the lens and the posterior surface of the band of disjunction (fig 1A and table, column A)
- B Those between the posterior surface of the band of disjunction and the region of the

anterior Y suture (fig 1A and table, column B)

- C Those in the region of the anterior Y suture, including that section of the lens lying between the anterior fetal nuclear band and the anterior surface of the central dark interval (fig 1B and table, column C)
- D Those in the central dark interval itself
- E Those in the region of the posterior Y suture, including the area from the central dark interval up to and including the posterior fetal nuclear band (fig 1B and table, column E)
- F Those between the posterior fetal nuclear band and the anterior surface of the posterior band of disjunction (table, column F)
- G Those from (and including) the posterior band of disjunction to the posterior surface of the lens. (table, column G)

The eyes were also divided into two groups, those with few opacities (F) and those with numerous opacities (N) (table, column H). Capsular pigmented stars (P S) and persistent pupillary strands (P M) were noted (table, column I).

OBSERVATIONS

Only 8 of the 300 eyes examined were entirely free of opacities of the lens. All others showed punctate opacities in one or more sections of the lens. Because of the difficulty of differentiating between congenital and presenile forms of punctate opacities, the latter were considered to be physiologic and were included in this survey.

Sixty-eight eyes (23 per cent) contained opacities in the region between the anterior band of the lens and the posterior surface of the anterior band of disjunction. Somewhat deeper in the lens (between the band of disjunction and the region of the anterior Y suture) opacities were much more numerous, being present in 227 eyes (76 per cent). In the central portions of the lens the opacities diminished in number (44 eyes,

1 Pellaton, R. Die physiologischen Linsentrübungen im Kindesalter nach Spaltlampenuntersuchung an 164 normalen Kinderaugen, Arch f Ophth 111:341-351, 1923.

2 Vogt, A. Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges, Berlin, Julius Springer, 1930-1931.

3 Walther, cited by Norris, W F, and Oliver, C A. A Textbook of Ophthalmology, Philadelphia, Lea Bros & Co, 1893.

Location of Opacities in the Crystalline Lens

Patient	Age yr	Sex	Eye	A*	B	C	D	E	F	G	H	I	Comment
1	25	♂	1	1	+				+		N		Bilateral coronary and cerulean cataracts
			2	2	+				+		N		Bilateral coronary and cerulean cataracts
2	18	♂	3	4				+	+			F	
			4										Clear
3	28	♂	5	6	+							F	Clear
			7										
4	36	♂	8	9	+	+	+		+	+	N		Opacities most numerous nasally
			10								F		Nuclear relief
5	35	♂	11	12	+	+		+	+	+	F		Nuclear relief
			13								F		Opacities situated nasally
6	21	♂	14	15	+			+			F		Opacities situated nasally
			16								F		
7	37	♂	17	18	+				+	+	N		Nuclear relief marked opacities most
			19								N		numerous nasally in both lenses
8	27	♂	20								N		
9	20	♂	21	22	+			+	+	+	F		
10	30	♂	23	24							F		Lens clear
			25										Lens clear
11	25	♂	26	27	+				+		N		
			28								F		Coronary cataract
12	18	♂	29	30	+	+	+		+	+	H		Coronary cataract
			31										
13	19	♂	32	33	+						F		Few streaks in periphery also present
			34								F		Few streaks in periphery also present
14	18	♂	35	36	+	+	+		+	+	F		Single punctate and linear opacities in
			37								F		lower nasal quadrants
15	20	♂	38	39	+						F		Punctate opacities situated nasally
			40								F		Opacities situated entirely nasally
16	20	♂	41	42	+	+	+		+	+	F		Opacities situated entirely nasally
			43								F		
17	38	♂	44	45	+	+					F		Opacities situated in periphery particularly
			46								F		nasally
18	20	♂	47	48	+	+			+	+	F		Lens clear
			49								F		Bilateral punctate opacities on the anterior
19	21	♂	50	51	+						F		cortical suture system
			52								F		
20	27	♂	53	54	+	+					F		Opacities situated mainly nasally
			55								F		Opacities situated mainly nasally
21	22	♂	56	57	+	+					F		Opacities situated mainly nasally
			58								F		Opacities situated mainly nasally
22	24	♂	59	60	+						F		Opacities situated mainly nasally
			61								F		
23	27	♂	62	63	+	+			+	+	F		Opacities in periphery
			64								F		
24	25	♂	65	66	+		+				F		P S
			67								F		Cataracta cerulea
25	37	♂	68	69	+	+					F		Opacities situated entirely nasally
			70								F		Opacities situated entirely nasally
26	31	♂	71	72	+	+			+	+	F		Opacities situated mainly nasally
			73								F		
27	19	♂	74	75	+	+			+	+	F		Several faint whitish linear opacities on
			76								F		anterior capsule
28	27	♂	77	78	+	+			+	+	N		Retrobulbar pigmented stripe on anterior
			79								N		lens surface of both eyes
29	27	♂	80	81	+	+			+	+	N		Anterior rosette shaped cataract (nontraumatic)

See text for interpretation of symbols

Location of Opacities in the Crystalline Lens—Continued

Patient	Age, Yr	Sex	Eve	V*	B	C	D	E	F	G	H	I	Comment
39	50	♂	77 78	+	+	-	-	+	+	-	F		
40	22	♂	79 80					+	+	-	F		
41	56	♂	81 82	+	+	+		+	+	+	N		• Opacities situated mainly nasally • Opacities situated mainly nasally
42	18	♂	83 84		+			+			I		
43	19	♂	85 86		+		+			-	F	P S	
44	22	♂	87 88		+		+		+		I		
45	27	♂	89 90		+	r	+				I	P S	
46	23	♂	91 92		+	+	+				I		Opacities situated inferiorly Opacities situated mainly nasally
47	27	♂	93 94		+		+			+	N		Opacities in both lenses more numerous posteriorly and inferiorly
48	21	♂	95 96		+	-	-		+		I		
49	34	♂	97 98		+		+				I		Nuclear relief
50	21	♂	99 100		-		+			+	I	P M	Opacities situated mainly nasally Opacities situated mainly nasally
51	28	♂	101 102		+	+		+	+		N		
52	31	♂	103 104		+	+		+	+		I	P S	
53	22	♀	105 106	+	+		+		+	+	I		Opacities situated mainly nasally Opacities situated mainly nasally
54	23	♀	107 108	+		+	+	+	+	+	I		
55	29	♀	109 110		+		+		+	+	I		Opacities situated mainly nasally 1 opacity on posterior surface
56	22	♀	111 112		+	+			+	+	F		Cortical opacities situated mainly nasally Cortical opacities situated mainly nasally
57	25	♂	113 114		+		+			+	I		
58	23	♂	115 116	+	-		+				N		
59	35	♀	117 118		+				+	+	N		Nuclear relief
60	15	♂	119 120	+	-		+		+	+	N		Anterior sutural extract (presenile type) and cuneiform opacities, same as 119 except cuneiform opacities absent
61	25	♂	121 122		+				+		I		Also shows 1 striate opacity situated nasally
62	20	♂	123 124		+	+		+	+		N	P S, P M	Anterior cortical opacities situated nasally
63	28	♂	125 126	+	+	+		+	+		N	P M	One linear opacity present inferiorly
64	40	♀	127 128	+	-		+		+	+	I	P S	Peripheral concentric lamellar and nuclear relief present in both eyes
65	34	♂	129 130	+	+			+	+		F		Wreath of faint lines on anterior lens surface of each eye
66	24	♂	131 132		+		+				F	P M	
67	21	♂	133 134	+		+			+		I	P S	Opacities situated mainly nasally
68	33	♂	135 136	+			+				F	P M	Pupillary strand extending from pupillary margin to opacity on lens surface
69	21	♂	137 138	+				+	+		F		Peripheral concentric lamellar opacities
70	23	♂	139 140	+				+	+	+	F	P M	
71	25	♂	141 142	+					+		F		Opacities situated mainly nasally and also inferiorly
72	23	♂	143 144	+					+	+	N	P S	Opacities situated nasally and inferiorly
73	26	♂	145 146	+		+		+	+		F		Opacities situated nasally and inferiorly
74	22	♂	147 148	+			+		+		F		Peripheral concentric lamellar opacities
75	34	♂	149 150	+	+	+	+	+	+		N		Peripheral concentric lamellar opacities
76	19	♂	151 152	+				+	+		F	P S	

* See text for interpretation of symbols

Location of Opacities in the Crystalline Lens—Continued

Patient	Age, Yr	Sex	Eye	A*	B	C	D	E	F	G	H	I	Comment
77	38	♂	153 154	+	+		+	+	+		N N	P S	Slight nuclear relief in both eyes
78	40	♂	155 156		+	+	+	+	+		N N		Most opacities situated inferiorly and nasally
79	21	♂	157 158	+	+			+	+		F F		
80	35	♂	159 160			+					F F		Incomplete stellate cataract in both eyes and some opacities situated nasally in left eye
81	38	♂	161 162		+					+	F F		
82	25	♂	163 164		+				+		F F		
83	22	♂	165 166		+		+				F F		Cortical opacities situated mainly inferiorly and nasally
84	36	♀	167 168		+				+		F F		Nuclear relief
85	36	♀	169 170						+	+	F F		Nuclear relief
86	26	♂	171 172		+		+		+		F F		Nuclear relief
87	24	♂	173 174			+	+				F	P S	Beginning coronary opacities
88	25	♂	175 176		+		+			+	F F	P S P M P M	
89	21	♂	177 178		+				+	+	F F		Opacities situated mainly nasally
90	25	♂	179 180	+	+				+	+	N N		Opacities situated mainly nasally
91	37	♂	181 182		+			+	+	+	F F		Beginning peripheral concentric lamellar opacities and coronary cataracts
92	29	♂	183 184		+	+	+	+	+	+	N N		Nuclear relief
93	18	♂	185 186		+				+	+	F F		Nuclear relief
94	20	♂	187 188		+	+			+		F F		Beginning bilateral opacities
95	23	♂	189 190		+		+				F F		Peripheral concentric lamellar opacities
96	27	♂	191 192		+			+		+	F F		Peripherally concentric lamellar opacities
97	26	♂	193 194		+				+	+	F F		Early peripheral concentric lamellar opacities
98	19	♂	195 196		+	+	+	+	+	+	F F		Early peripheral concentric lamellar opacities
99	26	♂	197 198	+	+				+	+	F F		Stellate opacities in both lenses
100	26	♂	199 200		+	+		+	+	+	N N	P S P M P S	
101	39	♂	201 202		+				+	+	N N		Peripheral concentric lamellar opacities
102	29	♂	203 204		+	+			+	+	N N		Opacities situated mainly nasally
103	31	♂	205 206		+				+	+	N N		Many fine punctiform opacities under anterior capsule deeper opacities situated mainly nasally
104	22	♂	207 208		+			+	+	+	F F		Opacities situated mainly nasally
105	33	♂	209 210		+		+	+	+	+	F F		Opacities situated mainly nasally
106	23	♂	211 212		+				+	+	N N		Opacities situated mainly nasally
107	28	♂	213 214		+		+	+	+	+	N N		Cataracta cerulea
108	20	♂	215 216		+				+	+	N N		Cataracta cerulea
109	27	♂	217 218		+	+		+	+		F F		Opacities situated mainly nasally
110	24	♀	219 220		+			+		+	F F		Opacities situated mainly nasally
111	22	♂	221 222		+				+		N F		
112	23	♂	223 224		+			+	+	+	F F		
113	38	♂	225 226		+				+	+	N F		P M
114	35	♂	227 228		+				+	+	N F		A striate opacity also present nasally
													Opacities situated mainly nasally nuclear relief
													1 linear opacity and many punctate opacities situated nasally nuclear relief
													Opacities situated mainly inferiorly and nasally

* See text for interpretation of symbols

Location of Opacities in the Crystalline Lens—Continued

Patient	Age, Yr.	Sex	Eve	V*	B	C	D	I	I	G	H	I	Comment
115	40	♂	229		+	+					I		Triradiate opacities, other opacities situated mainly nasally, nuclear relief also present
			230		+	+					F		Triradiate opacities
116	21	♂	231				+				F	P M	Opacities situated mainly nasally
			232		+						F		Opacities situated mainly nasally
117	28	♂	233		+		+		+		N	P S	Opacities situated mainly nasally
			234		+						N		Opacities situated mainly nasally, also cataract cerulea present
118	18	♂	235					+			F		
			236					+	+		F		
119	28	♂	237		+	+	+		+		I		Krukenberg spindle on cornea, opacities in lens situated mainly nasally
			238										Lens clear
120	36	♂	239		—	—					F		Opacities situated mainly nasally also triradiate opacities
			240			—					F		Triradiate opacities
121	27	♂	241		+						F	P S	
			242		+						F		
122	29	♂	243		—	—					I		Opacities situated nasally
			244			—					I		
123	30	♂	245		+						N		Most opacities situated nasally in both eyes
			246		+						N		
124	25	♂	247	+	+						N		Cataracta coronaria and cerulea
			248	+	+						N		Cataracta coronaria and cerulea
125	26	♂	249	—	—						I		
			250	—	—						I		
126	40	♂	251	—	—						N		Cataracta coronaria
			252	—	—						N		Cataracta coronaria
127	27	♀	253		+						F		
			254			—					I		Both punctate and striate opacities situated nasally
128	23	♀	255		+						F		
			256		+						F		
129	27	♂	257	—							I		Opacities situated nasally and inferiorly
			258	—							N		
130	28	♂	169		—						I		
			260		—						F	P M	
131	24	♀	261								F	P S	
			262			—					F		Triradiate cataract
132	23	♀	263		—						N	P M	
			264		—	—					N		Peripheral concentric lamellar opacities
133	22	♀	265		—						I	P S	
			266		—						I		
134	24	♂	267								F		
			268			—					F		
135	22	♀	269		—						F		Opacities situated mainly nasally
			270		—						F		Opacities situated mainly nasally
136	23	♂	271		—						I		
			272		—	—					I		
137	29	♂	273		—	—					F	P S	Opacities situated entirely nasally
			274		—	—					F		Opacities in nasal portions
138	19	♂	275		—	—					N		Opacities in nasal portions
			276		—	—					N		Opacities situated mainly nasally
139	20	♂	277								I		Opacities situated mainly nasally
			278								I		
140	18	♂	279								F		
			280								F		
141	20	♂	281								I		Nasal opacity only
			282								I		
142	23	♂	283								N		
			284								F		
143	25	♂	285								F		
			286								F		
144	20	♂	287		—	—					F	P M	
			288		—	—					F		
145	29	♂	289								F		
			290								F		
146	21	♂	291		—						F	P M	Opacities situated entirely nasally
			292		—						F		Capsular opacity connected to pupillary strands
147	25	♂	293		—						F		
			294		—						F		
148	31	♂	295		—						N		Punctate opacity situated nasally
			296		—						N		Opacities situated mainly nasally also bilaterally
149	21	♂	297		—						F		Cataracta cerulea
			298		—						F		
150	21	♂	299								F	P S	Opacities situated mainly nasally
			300								F		

* See text for interpretation of symbols

or 15 per cent, had opacities in the anterior Y region 6 eyes, or 21 per cent, in the central dark interval and 56 eyes, or 19 per cent, in the posterior Y region) Like its anterior counterpart, the deep posterior cortex had numerous opacities (179 eyes, or 60 per cent, had opacities between the posterior Y region and the posterior band of disjunction) Finally, in the posterior

sections of the lens substance in all other eyes

Coronary cataracts were found bilaterally in 6 subjects (fig 2), in 2 of them the opacities were well developed and were associated with cataracta cerulea, while in 4 the coronary opacities were poorly developed Peripheral concentric lamellar opacities were present in 15 eyes (5 opacities being bilateral and 5 unilateral)

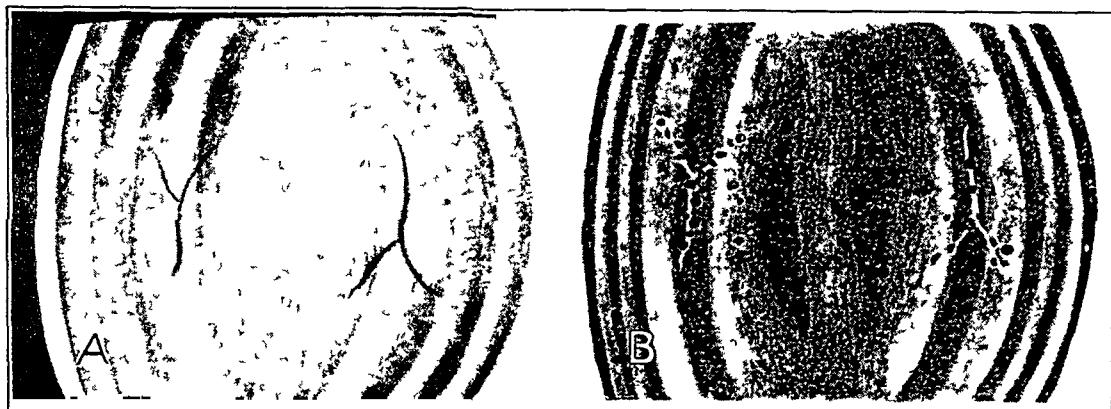


Fig 1.—*A*, punctate opacities in the upper portion of the anterior band of disjunction and axial opacities in the anterior and posterior adult nuclear bands. *B*, punctate opacities in the regions of the anterior and posterior Y sutures

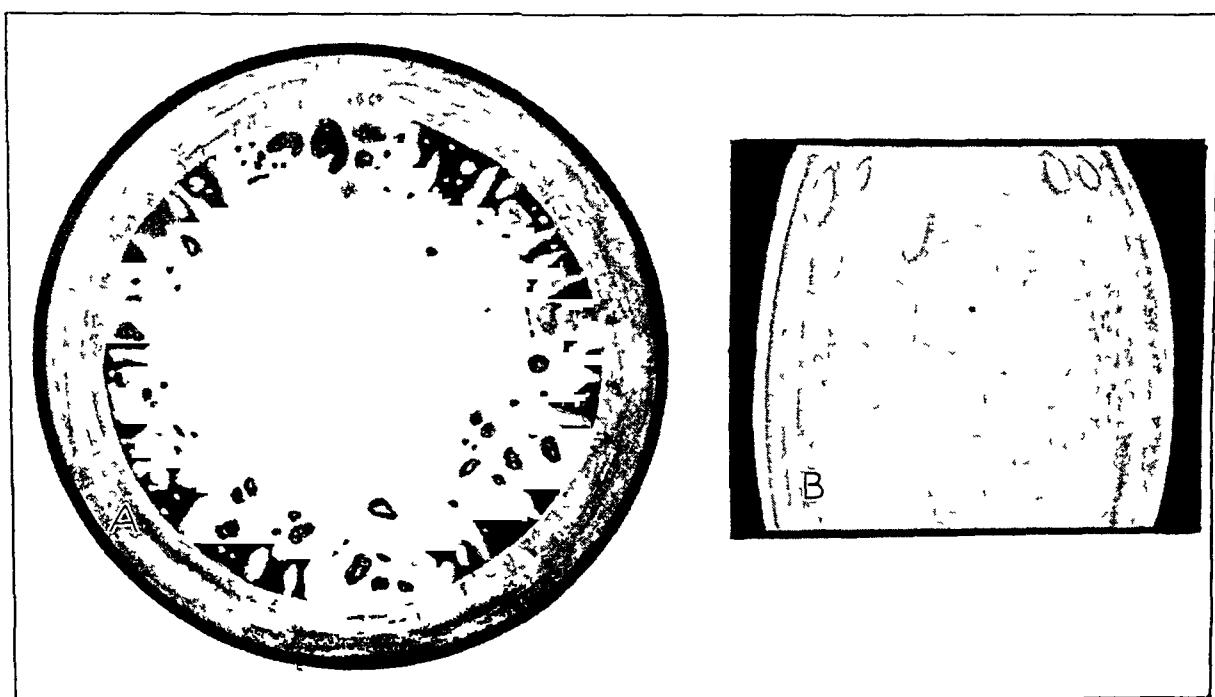


Fig 2.—Cataracta coronaria. *A*, ophthalmoscopic section, *B* optical section

superficial section the number of opacities decreased, approximating the number found in the corresponding anterior layer (70 eyes, or 23 per cent had such opacities)

In 65 eyes (22 per cent) the opacities were either exclusively or preponderantly in the nasal portions of the lens In 12 other eyes the opacities were mainly in the inferior and nasal portions The opacities were uniformly distributed peripherally or scattered throughout the various

Of 115 subjects (230 eyes) only 8 subjects (16 eyes) showed nuclear sclerosis and all the subjects in this group were over 35 years of age In 219 eyes opacities were few, the average age of the subjects having few opacities was 25 years Eighty-one eyes had numerous punctate opacities, the average age of the subjects was 30 years Nuclear relief was observed in 8 (16 eyes) of 115 subjects All persons showing nuclear relief were over 35 years of age

COMMENT

Nummular, annular and punctiform opacities measuring from 20 to 100 microns were found in all but 8 of 300 eyes examined with the slit lamp. Since these opacities increase in number with age, they must be considered forms of presenile cataract. However, opacities occur so commonly in otherwise healthy persons that their presence is considered normal. Cataracta coronaria, cataracta caerulea and cataracta vittata are included here because they are so frequently associated with presenile opacities.

Hess⁴ expressed the opinion that the site of predilection for incipient senile cataract is the immediate subcapsular layer. The present ob-

of this condition in this series was 26 years. A frequent associated finding was a widening and intensification of the anterior and posterior bands of the adult nucleus at the equator.

Punctate opacities following the pattern of the anterior axial system of cortical sutures may evolve into an opacity shaped like the antlers of a deer (fig. 3B). Punctate opacities on the anterior cortical suture system, as this form of presenile cataract is called, readily escape detection during a routine examination, even with a slit lamp, because the opacities are very minute. Vogt stated that the youngest patient observed by him with this type of cataract was 36 years of age. The condition illustrated in figure 3B

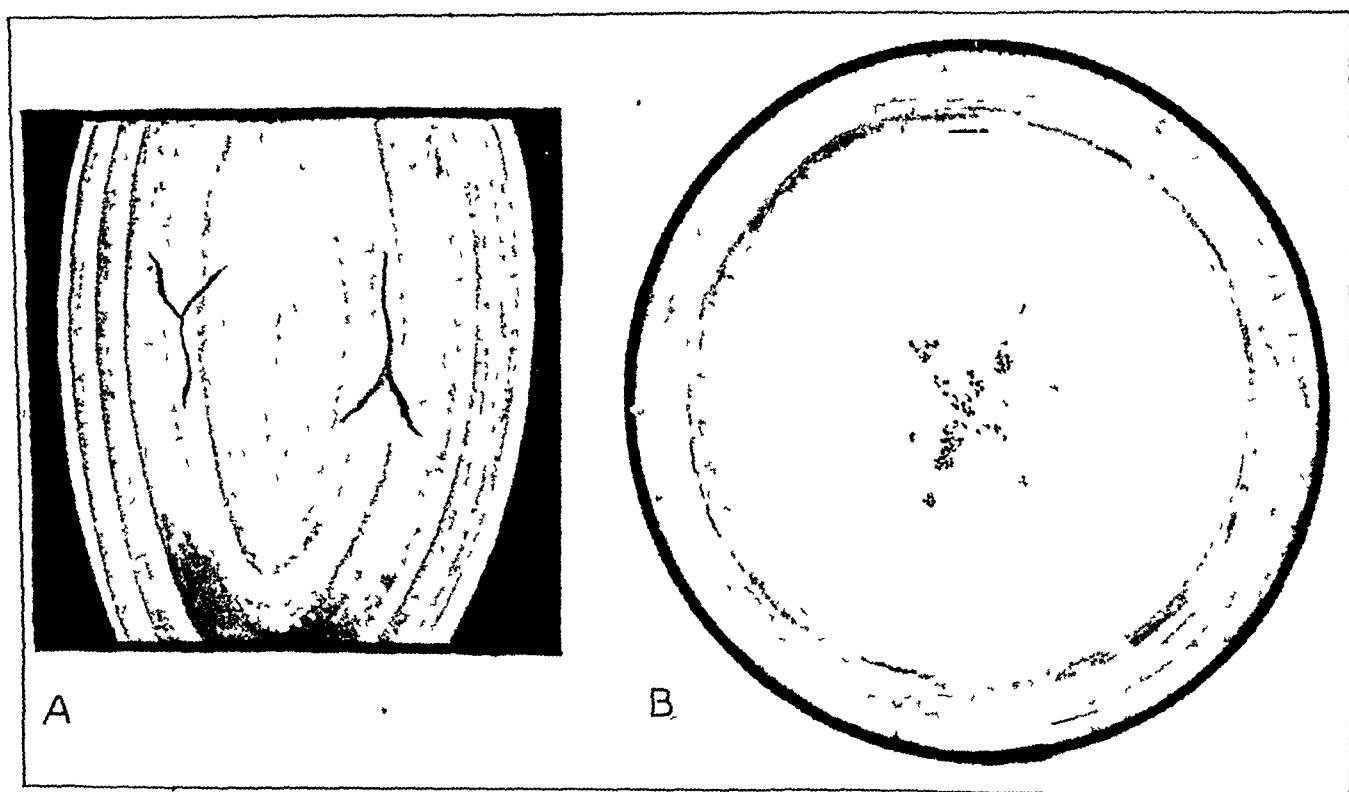


Fig. 3.—A, punctate opacities in the form of peripheral concentric lamellar layers. B, punctate opacities on the anterior cortical suture system.

servations indicate that the most common site of punctate opacities is between the band of disjunction and the region of the Y suture, particularly anteriorly. Later, as the lens ages, the opacities increase in number and involve the outer cortex. If the opacities are in the axial region and become dense, the visual acuity diminishes.

At times the punctate opacities in the periphery form concentric lamellar layers (fig. 3A). Vogt stated that an arrangement of large yellowish gray layers about the nuclear equator is found only in elderly subjects. The average age of the persons showing the incipient stage

was observed in a 25 year old soldier. That punctate opacities on the anterior cortical suture system are true forms of senile cataract is proved by the fact that cuneiform opacities, which are definitely a form of senile cataract, were also present.

Coronary opacities were present in 4 per cent of the eyes, a figure in close agreement with the results of the investigation by Kirby,⁵ who found that these opacities formed 4.5 per cent of all cataracts. Vogt, on the other hand, stated that coronary cataracts are found in 25 per cent of all persons past the age of puberty.

Case 38 (see table) raises the question of the causation of anterior rosette cortical cataract.

⁴ Hess, C., Pathologie und Therapie des Linsensystems, in Graefe, A., and Saemisch, E. T. Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, Wilhelm Engelmann, 1911, pt 2, chap 9.

⁵ Kirby, D. B. A Study of Standards for Judging of the Progress or Arrest of Cataract, Tr. Am. Acad. Ophth. 32:203-230, 1927.

This cataract is usually attributed to trauma. The subject of this report, a 27 year old soldier, said he had never received an injury to the involved eye. Slit lamp examination supported his contention, for objective signs of trauma were absent. Similar cases have been reported by Rauh,⁶ Nordmann⁷ and Handmann.⁸

Although this report concerns itself with opacities in the crystalline lens, the number of eyes showing pigmented capsular stars or pigmented strands was also noted (table, column I). Thirty-three eyes showed pigmented stars on the surface of the lens, and 23 showed pupillary strands. Gallemaerts and Kleefeld⁹ reported that embryonal pupillary remnants were observed by them in 20 per cent of all their cases. A tendency to absorption is indicated by the decreased incidence with age.¹⁰ One instance of pigmented

striae on the anterior surface of the lens in the retroiridal region was observed. The case referred to is included in another report.¹¹

SUMMARY

Three hundred eyes of persons between 18 and 40 years of age were examined by means of slit lamp microscopy. All but 8 eyes showed some form of punctate opacities. In 4 per cent of the eyes the opacities were associated with coronary cataracts. Punctate opacities were found in all the layers of the lens, but were far more common between the bands of disjunction and the region of the Y sutures, being more numerous anteriorly than posteriorly. Not uncommonly the opacities arranged themselves in concentric layers surrounding the nucleus. These opacities are precursors of peripheral concentric lamellar opacities of the senile lens, which are a true form of senile cataract. At times punctate opacities of unusually small size are present in the anterior cortical suture system.

CONCLUSIONS

Punctate opacities, which are found in nearly all adult lenses, increase in number with the age of the subject. They precede nuclear relief, increase in the elementary stripes composing the adult nuclear band and yellowing of the nucleus as a sign of aging of the lens.

11 Bellows, J. Pigmented Lines in Retroiridal Region of Anterior Capsule of Lens, Arch Ophth **32** 483-484 (Dec) 1944

6 Rauh, W. Blatt- oder rosettenförmige Starre, Klin Monatsbl f Augenh **84** 766-773, 1930

7 Nordmann, J. A propos de certaines formes de cataracte en rosace, Arch d'opht **48** 392-402, 1931

8 Handmann, M. Ueber den blatt- oder rosettenförmigen vorderen Rindenstar, eine nichttraumatische stationäre Starform unbekannter Ursprungs, Klin Monatsbl f Augenh **78** 31-43, 1927

9 Gallemaerts, E., and Kleefeld, G. L'étude microscopique du fond de l'œil vivant, Ann d'ocul **159** 264-274, 1922

10 Vogt² Hirschberg, J. Ueber langsame Rückbildung der persistirenden Pupillenhaut, Centralbl f prakt Augenh **28** 103-105, 1904 Bruckner, A. Ueber Persistenz von Resten der Tunica vasculosa lentis Arch f Augenh (supp) **56** 5-149, 1907 Bellows, J. Cataract and Anomalies of the Lens, St Louis C V Mosby Company, 1944

TOTAL HERPES ZOSTER OF THE OPHTHALMIC, MAXILLARY AND MANDIBULAR DIVISIONS OF THE TRIGEMINAL NERVE

REPORT OF A CASE IN WHICH THERE WAS ALSO INVOLVEMENT OF THE GENICULATE GANGLION AND THE VESTIBULAR PORTION OF THE EIGHTH CRANIAL NERVE

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Herpes zoster is a not rare acute infection of the posterior root ganglions with signs in the segmental distribution of the nerve roots involved,¹ while, contrariwise, herpes zoster ophthalmicus, or herpes zoster of a gasserian ganglion, a homologue of a posterior root ganglion, is apparently a rather rare disease, indeed, it is so rare that Rice² stated that no cases of ophthalmic herpes zoster were mentioned, for example, in the report of one of the largest ophthalmologic and otologic hospitals in the United States, in which over 100,000 patients with ocular disease were treated in 1922. On the other hand, Gundersen,³ in searching for cases of herpes zoster ophthalmicus, found 10 per annum at the Massachusetts Eye and Ear Infirmary, in Boston, over a five year period.

From the standpoint of the dermatologist, who will inevitably see ophthalmic herpes zoster initially, the common sites of localization of herpes zoster are an intercostal nerve, the trigeminal nerve (particularly the first branch, herpes zoster ophthalmicus) and the sensory nerves of the extremities. Herpes zoster of the arm or of the leg is unusual and hence often not diagnosed.⁴

Pillsbury, Sulzberger and Livingood⁴ stated that herpes zoster may occur as a concomitant manifestation with the leukemias, various blood dyscrasias, Hodgkin's granuloma and malignant visceral tumors and is not uncommon in tabetic syphilis. They grouped under the following five subdivisions the less common forms of herpes zoster: (1) gangrenous herpes zoster, with necrotic and destructive lesions, a severe form

1 Meakins, J C. *The Practice of Medicine*, ed 4, St Louis, C V Mosby Company, 1944

2 Rice, G W. *Herpes Zoster Ophthalmicus*, Eye, Ear, Nose & Throat Monthly **2** 265, 1923-1924

3 Gundersen, T. Convalescent Blood for Treatment of Herpes Zoster Ophthalmicus, *Arch Ophth* **24** 132 (July) 1940

4 Pillsbury, D, Sulzberger, M, and Livingood, C. *Manual of Dermatology*, Philadelphia, W B Saunders Company, 1943

of which can occur in any region but which is most common in the region of the ophthalmic nerve, (2) hemorrhagic herpes zoster, with blood-containing vesicles, (3) bullous herpes zoster, (4) bilateral herpes zoster, either symmetric or asymmetric, which is extremely rare but which, contrary to certain superstitions, is not fatal⁵, (5) generalized herpes zoster, in which the eruption consists of scattered discrete papules and vesicles and is accompanied by headache, fever and malaise. There may be lesions of the mucous membrane, with the entire picture resembling chickenpox. Only epidemiologic considerations and the presence of concomitant typical herpes zoster following the course of a nerve will permit differentiation between ordinary chickenpox and this type of herpes zoster.⁴

Herpes zoster is usually limited to one of the divisions of the fifth cranial nerve,⁵ although it rarely involves the nucleus of the sensory root of the seventh cranial nerve. This enabled Hunt⁶ to delineate the distribution of the cutaneous portion of the geniculate ganglion, since the herpetic cutaneous eruption is found in the area of distribution of that ganglion, that is, in the cleft between the ear and the face and on the membrana tympani, the auditory canal walls, the concha, the helix and antihelix and the tragus and antitragus. The cutaneous herpetiform response of the geniculate ganglion to herpes zoster apparently may be total or minimal. It can be stated dogmatically that herpes zoster involving not only the ophthalmic but the maxillary and mandibular divisions of the fifth cranial nerve is rare, judged by the total absence of reported cases in the literature. Axiomatically, total herpes zoster of the trigeminal nerve with concomitant cutaneous involvement of the geniculate ganglion, the combination of which likewise has not been

5 Grinker, R R. *Neurology*, ed 3, Springfield, Ill, Charles C Thomas, Publisher, 1943

6 Hunt, J R. *Herpetic Inflammation of the Geniculate Ganglion*, *J Nerv & Ment Dis* **34** 73 (Feb) 1907

reported in the literature, is rare indeed, although Fuchs, cited by Graves,⁷ reported 2 cases in which with herpes zoster ophthalmicus, that is, with manifestations of the frontal branch only, there was concurrent involvement of the seventh cranial nerve with resulting lagophthalmos and keratitis. This combination is not rare, nor is that of herpes zoster ophthalmicus with involvement of the third, fourth, sixth and seventh cranial nerves with ocular palsy. Cases of this condition have been reported fairly frequently. Moore⁸ found that in his cases in which herpes zoster was associated with ocular palsy involvement of the third cranial nerve was by far the most common phenomenon, viz., in 74 per cent.

At this point it is worth while to draw attention to an equivocal report of Agnello,⁹ who, in discussing 3 cases of herpes zoster, described in 1 a papular eruption of the forehead, in a second vesicles on the skin in the middle of the forehead and in a third vesicles on the left side of the face and forehead. He said that all three branches of the left trigeminus nerve were affected, a statement which is extremely hard to reconcile with the fact that no cutaneous herpetiform eruption along the maxillary and mandibular nerve trunks was described in his paper.

What, then, is herpes zoster? It occurs as two types, epidemic, idiopathic herpes zoster, arising, *de novo*, and symptomatic herpes zoster. The latter may be found in a patient, for example, with some antecedent factor, such as fracture of the basal portion of the skull, meningitis of syphilitic or tuberculous origin or tumor of the pons, in whom symptomatic herpes zoster then develops by reason of the virus, which the patient is carrying, attacking the injured fifth cranial nerve, the gasserian ganglion or the central connections of the fifth cranial nerve. There is, to be sure, no difference between the causal virus of the idiopathic and of the symptomatic type except that in the epidemic type the attack arises spontaneously in unprepared soil while in the symptomatic type preexisting trauma to the nerve is postulated.⁷ In the latter type, then, the virus has a fertile soil in which to thrive.

Brain reported symptomatic herpes zoster as a sequela of subarachnoid hemorrhage, while other writers incriminated such variants as pneumonia.

⁷ Graves, B., in Berens, C. *The Eye and Its Diseases*. Philadelphia, W. B. Saunders Company, 1936.

⁸ Moore, R. F. Ocular Manifestations of Lesions of the Fifth Cranial Nerve, *Brit M J* 2 783 (Oct 29) 1932.

⁹ Agnello, F. Clinical Varieties and Ocular Lesions of Herpes Zoster, *Riv oto-neuro-oftal* 11 172 (March-April) 1934.

carbon monoxide and arsenic as etiologic factors. In all cases of trigeminal herpes zoster, whether of the idiopathic or the symptomatic type, however, one thing is certain, that the ophthalmic branch is always involved and the other branches with extreme rarity. If cutaneous herpetic involvement were the whole story, the disease could well fall within the province of the dermatologist, but, unfortunately, intraocular complications occur in 60 per cent of the cases, with the cornea allegedly affected in 35 per cent of these. Graves,⁷ indeed, expressed the opinion that slit lamp examination would reveal deep epithelial changes in practically all cases, hence the importance of the disease to ophthalmologists is apparent.

HISTORICAL REVIEW

A short review of the historic aspects of the disease may not be amiss. In 1866 Hutchinson¹⁰ published his classic description of the disease, while a year later Bowman¹¹ described several cases of herpes frontalis seu ophthalmicus, with illustrations in 1 case, showing residual facial pitting and scarring. In a second case described by Bowman diplopia occurred, while in a third case one sequel was atrophy of the optic nerve. Bowman in his writings stressed the fact that the supraorbital and supratrochlear divisions of the frontal branch of the ophthalmic division of the trigeminal nerve are most commonly involved, with the nasociliary branch of the ophthalmic nerve usually escaping.

In Hutchinson's day the disease was confused with erysipelas as it is today, for that matter. Hutchinson's dictums on this point were in the eighties popular examination questions in the hospitals in London. These dictums bear repetition after some seventy-eight years:

Herpes frontalis is always limited to one side. It never transgresses the median line of the forehead and nose. It never affects the cheek although there may be some sympathetic oedema of contiguity. There is less general swelling of the skin than in erysipelas, much more pain and less constitutional disturbance in herpes than in erysipelas.

A corollary of this dictum followed, which stated that "if there is involvement of the nasociliary nerve and vesicles form on the side of the nose the eye is most likely to be involved," a statement which has been valid in 6 cases seen.

¹⁰ Hutchinson, J. Clinical Report on Herpes Zoster Frontalis, *Roy London Ophth Hosp Rep* 5 191, 1865-1866, Exact Portion Affected by Herpes, *ibid* 6 48, 1867.

¹¹ Bowman, W. Cases of Zoster, *Roy London Ophth Hosp Rep* 6 1, 1867-1869.

by me since 1939 but the universality of which has been denied. Not so noteworthy is Hutchinson's other statement that when the tip of the nose is involved the eye will be lost—a conclusion which was not validated by Friedenwald¹² or in my present case, in which the nose, tip and all both "within and without," was involved.

Another dictum that zoster never affects the cheek, apparently stood unchallenged until 1900, when Head and Campbell¹³ reported a case of idiopathic herpes zoster involving the mandibular branch in which the cutaneous manifestation did, obviously, affect the cheek. And sixty years after the enunciation of Hutchinson's dictum, Paton¹⁴ reported a case in which the herpetiform eruption affected both the forehead and the cheek the first and second divisions of the trigeminal nerve being cutaneously involved. Obviously, then, with the two exceptions noted, one in 1900 and the other in 1926, if Agnello's equivocal, and not easily interpreted report is dismissed trigeminal herpes zoster meant, in effect, zoster with a herpetiform eruption along the course of one or more of the three branches of the ophthalmic division of the trigeminal nerve only, that is, the lacrimal, the frontal (supraorbital and supratrochlear) and the nasociliary nerves. In the case presented in this paper in which all three of the divisions of the trigeminal nerve, the ophthalmic (lacrimal, frontal [supratrochlear and supraorbital] and nasociliary), the maxillary and the mandibular, exhibited cutaneous manifestations, there was not only concomitant erythema and herpes (Hunt's herpes) due to involvement of the geniculate ganglion but some preceding evidence of involvement of the vestibular branch of the eighth cranial nerve with the patient displaying symptomatic manifestations of tinnitus, nystagmus and partial loss of balance. After a review of the literature, therefore, I feel that in the case to be presented the neuro-ophthalmologic features are unique enough to interest ophthalmologists.

The age incidence of herpes zoster ophthalmicus has been stated to be 55 years (Lodge and Lodge¹⁵). In 6 cases observed by me in private practice in the past five years, 5 patients were under 45 years and 1 was a woman of 70 years. Fishei (cited by Paton) observed

12 Friedenwald, J S Report of Case of Herpes Zoster Ophthalmicus Treated with Convalescent Serum, Bull Johns Hopkins Hosp **45** 103 (Aug) 1929

13 Head, H., and Campbell, A W The Pathology of Herpes Zoster, Brain **23** 353, 1900

14 Paton, L The Trigeminal and Its Ocular Lesions, Brit J Ophth **10**.305 (June) 1926

15 Lodge, S, and Lodge, W Herpes Zoster Ophthalmicus, Tr Ophth Soc U Kingdom **43** 659, 1923

the condition in an infant 4½ months old, and Koch,¹⁶ in reporting in 1939 on a patient aged 5½ years, mentioned that this was the earliest age at which the condition had been observed at the Mayo Clinic. The impression is general that ophthalmic herpes zoster occurs most commonly in aged and debilitated persons. In my limited experience this has not been the case.

The patient in the case to be presented was 44 and a working man in extremely robust health with no known exposure to varicella, in but 1 case in my recent experience could the victim be classed as either aged or debilitated, and in no single case was a previous history of contact with varicella found despite questioning

ANATOMIC CONSIDERATIONS

The trigeminal nerve is made up of both motor (to muscles of mastication) and sensory roots and is therefore a mixed nerve. Root fibers from the second division mainly descend to the second cervical segment via the pons and the medulla, with the fibers from the ophthalmic division descending most caudad. The gasserian, or trigeminal, ganglion, which is a primary sensory and trophic station, lies on the pars petrosa of the temporal bone in the middle fossa in the floor of the lateral part of the cavernous sinus, and divides into the ophthalmic branch, with the associated ciliary ganglion, the maxillary branch, with the associated sphenopalatine ganglion and the mandibular branch with the associated otic and submaxillary ganglia. The sphenopalatine ganglion, which supplies the mucous membranes of the nose and palate is connected with the seventh cranial nerve, while the geniculate ganglion, from which the sensory root of the facial nerve arises, is in much more direct connection with the seventh cranial nerve than with the eighth cranial nerve, with which it communicates by the small branch known as the pars intermedia. The trigeminal nerve itself is related to the seventh cranial nerve by means of the superficial petrosal nerves the large and the small. The ophthalmic division of the trigeminal nerve innervates the lids conjunctiva, iris, cornea and root of the nose, while the external ear is innervated not only by the fifth cranial nerve but by the seventh cranial nerve, the internal meatus being supplied by the seventh and the posterior wall of the external acoustic meatus by the tenth cranial (vagus) nerve. The maxillary nerve transmits sensibilities from the cheeks, nasal fossa, palate and upper teeth. The mandibular nerve brings in sensibili-

16 Koch, F L P Herpes Zoster Ophthalmicus, Arch Ophth **21** 118 (Jan) 1939

ties from the chin, lower teeth, tongue and temporal region. Within the semilunar ganglion a rearrangement of fibers from a somatotopic to a physiologic plan occurs, and when the trigeminal tracts course through the medulla they carry specific types of sensibility from all the peripheral area.¹⁷ The peripheral fibers of the seventh cranial nerve (facial) after arising in the geniculate ganglion are incorporated in the chorda tympani and come from the taste buds of the anterior two thirds of the tongue. Efferent fibers arising in the medulla are incorporated with the sensory root to form the composite glossopalatine nerve. Through the chorda tympani these efferent fibers supply the submaxillary ganglion which supplies the submaxillary gland.¹⁷

The seventh nerve, then, is much more intimately connected with the geniculate ganglion than with the eighth nerve, for which reason facial paresis is much more common in herpes zoster than is symptomatic involvement of the vestibular branch of the eighth nerve.

PATHOLOGIC CONSIDERATIONS OF HERPES ZOSTER

Primary neuritis of the trigeminal nerve, if one excludes tic douloureux and neuralgia, is rare.¹⁸ The ophthalmic division of the trigeminal nerve, however, is especially apt to be affected by aneurysms of the carotid artery and by thrombosis of the cavernous sinus, while the trigeminal nerve as a whole may be involved by gummatous syphilis, basilar meningitis, fracture of the skull, tuberculosis and vascular pontile disease. As previously stated, there are two recognized types of the disease, a primary idiopathic involvement of the ganglions, occurring in either epidemic or sporadic form, and a symptomatic type, which appears during the course of an infectious disease, such as encephalitis (rare), or by extension by contiguity into the ganglion of a neighboring pathologic process. The virus of herpes zoster has apparently never been transmitted to animals.⁷ The herpetiform cutaneous lesions are probably due to antidromic impulses which cause the liberation of histamine-like bodies, and axon reflexes allegedly cause the spread of the vaso-dilatation.¹⁹ In this field of the viruses much remains to be learned. Is there a neurotropic as well as a dermatropic virus? Other unknown factors are the effect of resistance of tissue and the toxic effect of viruses, ignorance of which

beclouds the picture. Is it possible that in dendritic keratitis, keratitis disciformis, herpes corneae and herpes zoster ophthalmicus herpetic viruses play a part?⁷ Gruter, cited by Graves,⁷ demonstrated a specific herpes virus, which when transferred from a herpetic lesion in man to a rabbit's cornea produced a vesicular lesion, the virus, it is believed, travels by way of the fifth nerve to cause encephalitis. It has long been surmised that varicella and herpes zoster are related, and with increasing knowledge of the viruses it has been assumed that for idiopathic herpes there is probably a transmissible virus possibly related to varicella.²⁰ Bokay, in 1888, noted a case of varicella occurring ten days after the patient's contact with herpes zoster. Pickard²¹ expressed the opinion that the virus causing varicella and herpes zoster shows two phases, one representing herpes zoster and the other varicella. The zoster phase has its origin in a posterior root ganglion (it may spread to an anterior root, giving rise to the unusual muscular paralysis of herpes zoster), with extension and signs along the sensory nerves to fibrous tissue covered with epithelium, where the secondary or varicella phase appears. Blatt, Zeldes and Stein,²² at the Cook County Hospital, Chicago, noted varicelliform eruptions with pyrexia in 4 of 140 children in two wards thirteen to twenty-one days after exposure to patients with herpes zoster. The authors were in doubt of the identity of the viruses, but they agreed with many former workers that there is a close relationship between herpes zoster and varicella. In none of my 6 recent cases has any antecedent contact with varicella been found, nor has varicella developed in any of the children who come in contact with patients with herpes zoster. The secondary cutaneous lesions of herpes zoster always show lymphocytic invasion, hemorrhage, epithelial necrosis and large vesicular cells of Unna, while primary herpes is an inflammatory disease of the ganglion with lymphocytic infiltration, swelling of the axis-cylinders and destruction of the nerve cells. If the pathologic process is sufficiently grave, a secondary Wallerian degeneration occurs both in the dorsal roots and in the peripheral nerves. The ganglionic inflammation is therefore acute posterior poliomyelitis.¹³

17 Mettler, F A. Neuro-Anatomy, St Louis, C V Mosby Company, 1942.

18 Wechsler, I S. Textbook of Clinical Neurology, ed 5, Philadelphia, W B Saunders Company, 1943.

19 Parsons, J. Diseases of the Eye, ed 7, New York, The Macmillan Company, 1935.

20 Brain, R W. Zoster, Varicella and Encephalitis, Brit M J 1 81 (Jan 17) 1931 Head and Campbell¹³

21 Pickard, R. The Causation of Herpes Ophthalmicus, Proc Roy Soc Med 28 29 (Nov) 1934

22 Blatt, M L, Zeldes, M, and Stein, A F. Chicken Pox Following Contact with Herpes Zoster, J Lab & Clin Med 25 951 (June) 1940

Involvement of the eye of the affected side is usually explained by assuming that the disease extends by way of the long ciliary nerves which are given off from the nasal branch of the ophthalmic nerve, and thence, joining the short ciliary nerves from the ciliary ganglion, they pierce the sclerotic coat of the eyeball and pass forward between it and the choroid to the ciliary muscles, iris and cornea,²³ with keratitis, iritis, iridocyclitis and panophthalmitis as possible sequelae. Optic neuritis as a sequela of herpes zoster ophthalmicus is rare, for since Hutchinson's original report, in 1866, Duke-Elder²³ has collected only 10 reports of optic neuritis following herpes zoster, it occurred in 4 of 6 cases which I observed and studied. One wonders, therefore, if the difficulty of examining an acutely inflamed painful eye affected with herpes zoster does not explain this insignificant number of reported cases of involvement of the optic nerve. Gardilčić²⁴ described a case of herpes zoster in which, after the cornea of the eye was gravely involved, the eye became secondarily infected and a large hypopyon developed. Panophthalmitis resulted, and the eye was enucleated. Histologic study of this eye revealed that the small stumps of the ciliary nerves had an infiltration of plasma and small round cells, these infiltrated the sclera and the suprachoroida and were scattered through the choroid. Furthermore, the ciliary blood vessels near the nerves were also surrounded by lymphocytes and plasma cells, there were two areas of necrosis in the sclera, which were stated by the author to be due to trophic disturbances in the diseased nerves.

Valière-Vialeix found that in 13 of 17 cases superficial keratitis with vesicular formation was rare while, on the other hand, the posterior and middle layers of the corneal stroma were affected.²⁵ Keratitis profunda, in short, was the common, rather than the rare, lesion, while in 1 case in their report there was also an Argyll Robertson pupil with no response to light but with retention of reaction to convergence. The Argyll Robertson pupil following herpes zoster is usually dilated, according to Wolff.²⁶

23 Duke-Elder, W S Textbook of Ophthalmology, St Louis, C V Mosby Company, 1941

24 Gardilčić, A Perineuritis and Periarteritis Ciliaris in a Recent Case of Herpes Zoster Ophthalmicus, *Ztschr f Augenh* **92** 35 (May) 1937

25 Valière-Vialeix, V Frequency of Parenchymatous Keratitis in Herpes Zoster An Argyll-Robertson Pupil as a Sequel of Herpes, *Ann d'ocul* **168** 341 (May) 1931

26 Wolff, E The Pathology of the Eye, Philadelphia, The Blakiston Company, 1943

Carmody,²⁷ in discussing the complications of herpes zoster ophthalmicus, classified them in four groups keratitis, iridocyclitis, muscular palsies and optic neuritis. In 50 per cent of the cases, according to Carmody, the globe was affected, and in the majority of these the cornea was damaged. He reported an interesting case in which herpes zoster ophthalmicus on the right side in a 40 year old syphilitic Negro was followed in three weeks by exophthalmos on the same side, which produced immobility of the globe. The cornea was severely involved, in this case one cannot be certain, of course, whether the condition was of the epidemic (idiopathic) type occurring in a syphilitic patient or whether it was of the symptomatic type due to syphilitic basilar meningitis, or possibly a gummatus process of syphilis.

Paralysis and atrophy of muscles, not necessarily related to the course of the cutaneous herpetic eruption, in cases of herpes zoster were reported by Taterka and O'Sullivan.²⁸

The paralysis allegedly may occur as late as two months after the appearance of the herpetic eruption.

Denny-Brown and his co-workers²⁹ discussed the pathologic features of herpes zoster in 3 cases. In 2 cases of thoracic herpes zoster they reported in addition to severe neuritis degeneration of the involved motor and sensory roots, localized leptomeningitis and homolateral segmental poliomyelitis. In a third case of geniculate herpes in which the cutaneous manifestations involved the auriculo-occipital region they found necrotizing ganglionitis of the second cervical ganglion, homolateral segmental posterior poliomyelitis in the cervical portion of the cord and an inflammatory reaction in the medulla with motor neuritis of the facial nerve. In the geniculate ganglion itself no cellular destruction was seen, but in fibers of the paraganglionic facial nerve some lymphocytic infiltration was observed.

TREATMENT OF HERPES ZOSTER OPHTHALMICUS

For acute cutaneous lesions apparently any dry antiseptic powder, preferably sulfathiazole, will do. Medicaments are legion. Meakins,¹

27 Carmody, R F Herpes Zoster Ophthalmicus Complicated by Ophthalmoplegia and Exophthalmos, *Arch Ophth* **18** 707 (Nov) 1937

28 Taterka, J H, and O'Sullivan, M E Motor Complications of Herpes Zoster, *J A M A* **122** 737 (July 10) 1943

29 Denny-Brown, D, Adams, R, and Fitzgerald, P Pathologic Features of Herpes Zoster Note on "Geniculate Herpes," *Arch Neurol & Psychiat* **51** 216 (March) 1944

following Sidlick³⁰ suggested intramuscular injections of solution of posterior pituitary (0.5 to 1 cc). He also suggested intravenous injections of sodium iodide, 10 cc of the 20 per cent solution, repeated on the second, fourth and seventh days. This method was used by Ruggles. Solution of posterior pituitary obviously should be used with caution as most patients with herpes zoster are reputedly elderly with presumably an already impaired cardiac apparatus. Pillsbury suggested heavy doses of vitamin B complex and vitamin E.⁴ Diphtheria antitoxin in doses of 5,000 units injected every two days if necessary, was suggested by the Walkers.³¹ Convalescent serum has been employed by both Friedenwald¹² and Gundersen.³ The latter suggested the injection of 200 to 400 cc of herpes zoster convalescent blood, the treatment should be initiated preferably before ocular infection occurs. Green³² suggested autohemotherapy. Five to 10 cc of whole blood removed from the antecubital vein, is injected into the gluteal region, every other day, accompanied by administration of 25 mg of thiamine hydrochloride twice a week for six injections. Lillie,³³ in presenting 3 cases of herpes zoster, enthusiastically supported the therapeutic use of smallpox vaccine, a remedy which has been employed in past years by Green³⁴ and others in the treatment of herpes simplex and dendritic ulcer. As can be seen, many of these therapeutic suggestions for treating a disease of unknown but of suspected virus origin border on the irrational, although, as Friedenwald¹² sagely observed cases of herpes zoster ophthalmicus are all too rare in the practice of any ophthalmologist to afford an adequate basis for the testing of diverse forms of therapy. For postherpetic pain roentgen irradiation of the gasserian ganglion and pons has been recommended⁵, application of high voltage roentgen rays to the back in the region of the posterior nerve root, injection of alcohol or section of the sensory pos-

terior root and section of the spinothalamic tract, which conveys impulses of pain from the involved area, are other suggestions.¹ All these methods have their proponents, but the problem of postherpetic pain has certainly not been solved. Peet³⁵ stated that postherpetic pain often persists for years especially in aged persons, with symptoms identical with those described in many cases of tumor of the gasserian ganglion. He reported 2 cases of postherpetic trigeminal neuralgia in which there was persistence of pain after section of the sensory root of the gasserian ganglion, complete permanent relief, therefore so certain with surgical treatment of major trigeminal neuralgia cannot be assured the victim of herpes zoster with postherpetic pain. The anatomic basis of this clinical finding rests on the fact that a degree of cephalic sensitivity, particularly pain, may be preserved even though the semilunar ganglion of Gasser is entirely removed, for the sensory fibers accompany the cervical sympathetic plexus on the carotid artery and ultimately enter the cord in the region of the first thoracic segment.¹⁷

REPORT OF CASE

R. W., a man aged 44, presented himself June 29, 1944 with manifold complaints of burning pain in the right ear, a feeling of inability to balance himself, nausea and diplopia. His past medical history was non-contributory, there was no history of influenza or labyrinthitis. Neurologic examination showed diminished hearing in the right ear and horizontal nystagmus of both eyes with the fast component to the right. With these was a Romberg sign, with falling to the right. He said that this sense of imbalance had not been present prior to three days preceding his visit. No cerebellar symptoms were elicited, the pulse and respiration were both normal, and his temperature was slightly elevated. The referring physician was informed that the patient was probably suffering from an inflammatory process of the eighth cranial nerve and its vestibular ganglions, although a hemorrhage in the cerebellopontile angle could not be categorically dismissed. He was seen on the following day, June 30, at which time the nystagmus had diminished but the Romberg sign was still present. His complaint now was that he had severe pain in the right lower jaw and the right ear. At this time swelling of the postauricular and preauricular lymph nodes was obvious. The following day, July 1 the pain had advanced to the right side of the face and to the right side of the upper lip, and in the late afternoon a perceptible lag of the face was noticeable, combined with severe submaxillary adenopathy and overwhelming fetor oris. On this evening severe pain set in along the right brow and the right cheek and in the right inner canthal region. The following morning, July 2, the temperature was normal but there were extensive periorbital edema and severe episcleral injection. Tension of the right eye, taken at this time and again in the afternoon, was normal on both occasions.

30 Sidlick D M. The Use of Solution of Pituitary in Herpes Zoster, *Arch Dermat & Syph* 22:91 (July) 1930 cited by Sanford, G A. *Handbook of Ocular Therapeutics*, ed 2, Philadelphia, Lea & Febiger, 1937

31 Walker, J R., and Walker, B F. Specific Treatment for Herpes Zoster, *Arch Ophth* 20:304 (Aug) 1938

32 Herpes Zoster of the Eye, *Bull Pract Ophth* 14:11 (May) 1944

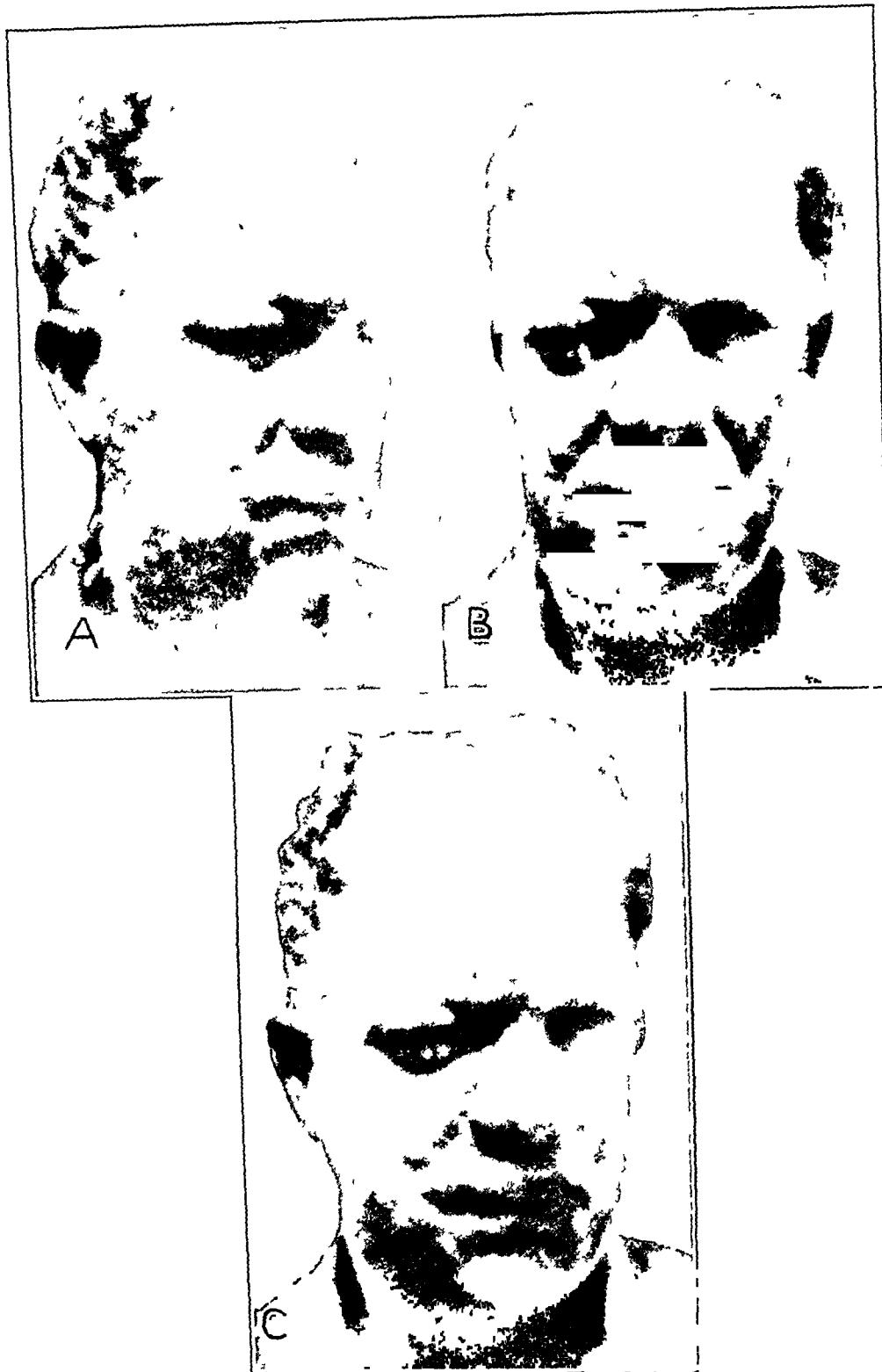
33 Lillie, W I. Treatment of Herpes Zoster Ophthalmicus with Smallpox Vaccine. *New York State J Med* 43:857 (May 1) 1943

34 Herpes Simplex of the Eye Prophylaxis with Use of Cowpox Vaccine. *Bull Pract Ophth* 13:27 (Nov) 1943

35 Peet, M M. Postherpetic Trigeminal Neuralgia. *J A M A* 92:1503 (May 4) 1929

There was much scleral tenderness, and now the right submaxillary gland was greatly enlarged and hard. Edema was present in the whole right half of the face, and the patient stated that the pain in the lower half of the face, in the roof of the mouth and in the jaw had diminished greatly but that the pain in the supraorbital and supratrochlear regions was more severe than ever. On the following day, July 3, a vesicular

eruption appeared on the soft palate, on the tongue and on the right side of the upper lip and on the tip and alar region of the nose. These lesions were too large and atypical to be dismissed as herpes febris. Examination of the ear on this day showed edema and a vesicular eruption of the posterior canal wall, with an extremely reddened, but not bulging, tympanum. There was some dental sepsis, and the pharynx was injected. On the



Snapshots of patient with herpes zoster. *A*, herpetic cutaneous lesions involving the ophthalmic branch of the trigeminal nerve (lacrimal, frontal [supraorbital and infratrochlear] and nasociliary), the cutaneous distribution of the right geniculate ganglion and the mandibular branch of the trigeminal nerve, severe submaxillary adenopathy and beginning involvement of the maxillary division of the trigeminus nerve are present. *B*, total efflorescence of herpetiform cutaneous lesions of the ophthalmic, maxillary and mandibular divisions of the trigeminal nerve. Involvement of the nasal tip is pronounced. According to Hutchinson (1866), this means the loss of the eye. Notice the ocular proptosis. *C*, generalized trigeminal cutaneous manifestation of herpes zoster. Preauricular and postauricular adenopathy, periorbital edema and exophthalmos are present. A few lesions involve the distribution of the maxillary division of the left side of the face. This is due to "crossing over" of the fibers of the maxillary division of the right side, a phenomenon which Paton pointed out is not rare in involvement of the ophthalmic division. Interestingly, there was no pain on the left side antecedent to this cutaneous vesication due to involvement of the maxillary division of that side.

following day, July 4, a magnificent herpetic eruption was present on the right side of the jaw and of the face, with severe erythema of the right cheek, forehead and right fronto-occipital region. The right side of the upper lip was now greatly swollen and vesicular, the fetor oris was worse, if possible, and the nystagmus and sense of imbalance (due to involvement of the vestibular part of the eighth nerve by connection of the geniculate ganglion with the eighth nerve) had disappeared. The right eye showed periorbital edema and exophthalmos with immobility, the cornea was insensitive to touch. Accordingly, the right pupil was dilated with instillations of 1 per cent atropine sulfate solution. The following day the diagnosis of herpes zoster ophthalmicus et maxillaris et mandibularis was obvious. Not so obvious now was the facial paresis (seventh cranial nerve) on account of the edema and the submaxillary adenitis. The cutaneous manifestation of herpes zoster oticus due to involvement of the geniculate ganglion, however, added one more bizarre feature to the picture in this miserable patient. The cutaneous vesiculation of the whole right side of the face, including the cleft between the face and the right ear, was extremely striking. During the following fifteen days, while the vesiculations slowly dried and scabbed, repeated slit lamp examinations of the eye revealed severe keratitis profunda, while repeated ophthalmoscopic examinations showed an inflamed nerve head with a cloudy posterior chamber. There was a moderate amount of ocular immobility, which could not be accurately tested for magnitude on account of the pain, the patient constantly complaining that his eye "was being pushed out." These ocular findings remained more or less static during the three weeks of disease. There was moderate optic neuritis throughout the illness. Visual acuity in the involved eye one month after the onset of the disease was 20/50. In my previous 6 cases of recent years all therapeutic measures which were employed seemed to be worthless and irrational. Whatever was done did little, if anything, to shorten the duration of the disease, consequently, in the present case it seemed that scrupulous local care of the eye and meeting emergencies, if and when they arose, could promise as much for the patient as a scatter shot attempt at battling the infection (of probable virus origin) with smallpox vaccine, autohemotherapy or convalescent blood therapy.

Consequently, no spectacular therapy was attempted apart from administration of heavy doses of salicylates by mouth, 80 grams (5 2 Gm) daily, 100,000 units of vitamin A daily by mouth, morphine sulfate hypodermically for pain, atropine sulfate and boric acid ointment to the eye and sulfathiazole powder to the vesicles. At the present writing the patient showed much residual scarring and pitting of the scalp, forehead, nose and face and complained of continuous mild pain, chiefly in the region of the ophthalmic division of the trigeminal nerve and in the roof of the mouth, as sequelae of a condition which was remarkable not only for the extent of the cutaneous nerve involvement but for the severity of localized pain and for the relatively minor involvement of the eye. It did indeed seem that the extent of the ocular involvement was inversely proportional to the severity of the herpetiform cutaneous manifestations.

SUMMARY

Herpes zoster of the trigeminal nerve universally affects the ophthalmic division of that nerve. Antidromic impulses originating in the semilunar ganglion allegedly cause the liberation of histamine-like bodies, which produce the vesicles. Why the ophthalmic branch alone is selectively affected is unknown. The frontal (supraorbital) branch of the ophthalmic division is always affected, the supraorbital branch nearly always and the nasociliary often. A review of the literature reveals but 1 reported case of idiopathic herpes zoster in which in addition to the ophthalmic nerve the mandibular nerve was affected (Head and Campbell, 1900). Likewise, 1 case was reported in which the ophthalmic and maxillary divisions of the trigeminal nerve were cutaneously involved (Paton, 1926). I found no report in the literature of a case of herpes zoster of the trigeminal nerve in which involvement of all three divisions occurred. A case of more than passing interest, then, to ophthalmologists is herein reported in which, combined with partial herpes zoster of the seventh cranial nerve (Hunt's) and preceding involvement of the vestibular ganglion of the eighth cranial nerve, complete herpes zoster involving all three divisions of the trigeminal nerve occurred. On account of the severe pain, the ocular involvement and the residual scarring on the cutaneous branches of the trigeminal nerve, a diagnosis of herpes simplex or of herpes febrilis is inadmissible. There were displayed in relation to the ocular condition optic neuritis, exophthalmos, keratitis profunda and probable mild involvement of the third, fourth and sixth cranial nerves. No evidence for classifying this case as one of symptomatic herpes zoster arising from encephalitis, syphilis, tuberculosis, leukemia, Hodgkin's disease, hemorrhage in the cerebellopontile angle or cerebral tumor was found. On the other hand, in view of the severe pain and the cutaneous herpetiform manifestations, the case is obviously one of idiopathic herpes zoster of the fifth (complete), seventh (partial) and eighth (vestibular) cranial nerves. All three snapshots reveal the magnificently vesicular efflorescence in various stages of herpetiform cutaneous response to involvement of the geniculate ganglion and of the ophthalmic, maxillary and mandibular divisions of the trigeminal nerve.

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OPHTHALMIC REQUIREMENTS OF THE MILITARY SERVICES

CHANGES FROM JAN 1, 1944 TO JAN 1, 1945

CHARLES A BAHN, MD

NFW ORLEANS

At the request of the American Committee on Optics and Visual Physiology, the following supplement is presented. For details, the reader is referred to the original articles.¹

ARMY, INCLUDING SELECTIVE SERVICE

- A For appointments in commissioned grades, no changes
- B For induction of enlisted personnel

Ophthalmologic Requirements According to Classes

Class	1	2	3
Visual acuity 20 ft (6 m)	20/20 in each eye	20/40 in each eye, correctable to 20/20, glasses to be worn	20/100 in each eye, correctable to 20/20 and 20/30, glasses to be worn
50 cm	Jaeger type 1, 50 in each eye	Jaeger type 6 at 50 cm in each eye, correctable at 50 cm to Jaeger type 1, glasses to be worn	Jaeger type 1 at 50 cm and Jaeger type 2 at 50 cm with correction, glasses to be worn
Depth perception at 6 m	30 mm maximum, uncorrected	35 mm maximum with correction	Pilots only 40 mm maximum with correction
Heterophoria Esophoria	10 mm maximum	10 mm maximum with correction	12 mm maximum with correction
Exophoria	5 pd maximum	5 pd maximum with correction	7 pd maximum with correction
Hyperphoria	1 pd maximum	1 pd maximum with correction	2 pd maximum with correction
Prism divergence	3-15 pd Divergence must equal or exceed esophoria	3-15 pd with correction	2-15 pd with correction, divergence must equal or exceed esophoria
Field of binocular rotation (red lens test)	No diplopia or suppression within 50 cm of primary position	No diplopia or suppression within 50 cm with correction	No diplopia or suppression within 30 cm with correction
Power of convergence	Pc must not exceed pd*	Pc must not exceed pd* with correction	Omitted
	Not less than minimum for age (see table)		OMITTED

TABLE OF MINIMUM VALUES OF ACCOMMODATION

Accommodation	Age	Diopters								
	17	8.8	23	7.5	29	6.0	35	4.3	41	2.4
	18	8.6	24	7.2	30	5.7	36	4.0	42	2.0
	19	8.4	25	6.9	31	5.4	37	3.7	43	1.5
	20	8.1	26	6.7	32	5.1	38	3.4	44	1.0
	21	7.9	27	6.5	33	4.9	39	3.1	45	0.6
	22	7.7	28	6.2	34	4.6	40	2.8		

Field of form

Contraction of 15° in any meridian disqualifies (normal limits temporally, 90°, superiorly, 65°, nasally, 60°, inferiorly, 75°). Disqualifying scotoma any except physiologic blind-spot on original examination, scotoma due to active process

Refraction

Maximum 1.50 D in any meridian, 0.50 D of astigmatism

Maximum 3.00 D in any meridian, 1.50 D of astigmatism

No maximum limits

* Pc indicates near convergence point, pd, interpupillary distance

From the Department of Ophthalmology, Medical Center, Louisiana State University School of Medicine

1 Bahn, C A. Ophthalmic Requirements of the Military Services, Arch Ophth 27:1202-1213 (June) 1942, 29:831 (May) 1943, 31:160-161 (Feb) 1944

- 1 General service (a) Binocular (both eyes open) vision of not less than 20/40 without glasses, provided the vision in the more defective eye is not less than 20/70 without glasses and provided the defective vision is not due to active or progressive organic disease
 (b) Visual acuity without glasses of not less than 20/200 in each eye, provided vision is correctable to 20/40 in each eye and provided the defective vision is not due to active or progressive organic disease. The actual possession of suitable glasses by an individual is not required for his acceptance under these standards²
- 2 Limited service (a) Minimum vision of 20/400 in each eye without glasses, correctable to 20/40 in one eye and 20/70 in the other eye, or 20/30 in one eye and 20/100 in the other eye

² Effective only from April 1944 to September 1944 general service. Visual acuity without glasses of not less than 20/200 in each eye or 20/100 in one eye and 20/400 in the second eye, provided vision is correctable to 20/40 in each eye, to 20/30 in one eye and 20/70 in the other eye or to 20/20 in one eye and 20/400 in the other eye, and provided the defective vision is not due to active or progressive organic disease. The actual possession of suitable glasses by a candidate is not required for his acceptance under these standards.

(b) Loss of one eye (anophthalmos) or any degree of defective vision in one eye from 20/400 to absence of light perception, if such defective vision is not due to active or progressive organic disease, with vision in the other eye of 20/100 without glasses, correctable to 20/20 with glasses

C Air Corps Flying

NAVY, MARINE CORPS, MERCHANT MARINE,
 COAST GUARD, AND UNITED STATES
 PUBLIC HEALTH SERVICE

No changes have been made. For requirements, see original articles¹

The committee acknowledges the cooperation and assistance of Surgeon General Norman T Kirk and Lieutenant Colonel G E Gorman, of the United States Army, Surgeon General Ross T McIntire, of the United States Navy, and Surgeon General Thomas Parran, of the United States Public Health Service.

The regulations supplementing the bibliography given in the original articles are contained in the following authorities:

Letter from Surgeon General of the Army, Jan 26, 1945

Letter from Surgeon General of the Navy, Jan 9, 1945,

Letter from Surgeon General, United States Public Health Service, Feb 8, 1945

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Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Bacteriology and Serology

RELATIONSHIP BETWEEN THE BACTERIOLOGY OF THE CONJUNCTIVA AND NASAL MUCOSA C BERENS and E L NILSON, Am J Ophth 27: 747 (July) 1944

Berens and Nilson found that 50 per cent of the 83 sets of cultures of material taken from the nasal and conjunctival membranes of 75 patients with extraocular diseases yielded organisms similar in type and toxicity for both the conjunctival and the corresponding nasal membranes, 43.3 per cent yielded "toxic" organisms in cultures of nasal secretions, with corresponding "negative" cultures of conjunctival material and approximately 3.5 per cent yielded organisms of slightly greater toxicity in cultures from the eye than in those from the nose.

In determining the etiologic factors of chronic and recurrent extraocular inflammatory diseases, it is advisable to investigate the nasal mucosa as a possible source of infection.

W S REESE

Biochemistry

THE METABOLISM OF THE CORNEA O S LEE, JR and W M HART, Am J Ophth 27: 488 (May) 1944

Lee and Hart give the following summary of their work:

"1 The normal epithelium of the cornea is shown to have a high oxygen uptake in contrast to a low uptake by the stroma. Because the endothelium consists of only a single layer of cells, it was impossible to measure its oxygen consumption by this method.

"2 The oxygen uptake of the corneal epithelium of riboflavin-deficient rats was found to be lessened. This may be accounted for by the cellular necrosis present in the epithelial cells of such corneas. When vascularization was present, the oxygen uptake by the stroma was found to be elevated, whereas in the absence of vascularization the oxygen uptake remained low. It is reasonable to assume that the increased oxygen uptake by the stroma is the result of vascularization and cellular infiltration.

"3 The metabolic activity of the xerotic cornea was found to be normal or higher than normal. The presence of metaplasia and hyperplasia instead of an actual cellular destruction of the corneal epithelium may be responsible for the approximately normal oxygen consumption of corneas of rats with vitamin-A deficiency."

W S REESE

Conjunctiva

SYPHILIS OF THE CONJUNCTIVA J L CASTILLO, Arch de oftal de Buenos Aires 18: 165 (March) 1943

Syphilis of the conjunctiva is rare. It may appear as a chancre, as simple conjunctivitis, as scleroconjunctival infiltration and pseudotrichoma of the tarsal conjunctiva and as gumma of the eyeball. There are no references in the literature to hereditary syphilis of the conjunctiva. A girl aged 10 years had subacute inflammation and infiltration of the cornea, which simulated tuberculosis. The Kahn reaction for syphilis was negative. The Mantoux test with a 1:1,000 dilution was strongly positive for tuberculosis. Antituberculosis treatment failed. Antisyphilitic therapy was administered because of the moderate hepatomegaly and splenomegaly, mild diffuse adenopathy and a high palate. The Kahn and Kline reactions became weakly positive in the course of antisyphilitic therapy. Rapid improvement and cure of the conjunctiva followed. The condition was diagnosed as hereditary syphilis of the conjunctiva.

J A M A (W ZENTMAYER)

Cornea and Sclera

VITREOUS STRIAE AND RETROCORNEAL TRABECULAE FOLLOWING INTERSTITIAL KERATITIS L SÁNCHEZ BULNES, Arch Asoc para evit cegueira México 1: 81, 1942

A woman aged 35, who had interstitial keratitis thirty years before, presented a V-shaped formation of corneal-vitreous striae and retrocorneal trabeculae with oblique illumination. Visual acuity was 6/10 in the right eye and 3/10 in the left eye.

The first description of these striae was given by Raehlmann, in 1877, and by Füldenbeig, in 1895. Füldenbeig stated that they were deposits of fat in the lymphatic spaces of the cornea.

Such vitreous striae may be adherent to the posterior corneal surface or may bridge out as trabeculae into the anterior chamber, fixed at either end to Descemet's membrane, and they occur in all types of interstitial keratitis. They must be differentiated from folds in Descemet's membrane.

Several hypotheses have been advanced to explain their formation:

(1) Cicatricial retraction of the corneal parenchyma takes place during the period of healing of the keratitis, forcing Descemet's membrane into folds into the anterior chamber; (2) the striae are residuals of a plastic inflammatory

process in the anterior chamber, and (3) folds of endothelial cells separate from Descemet's membrane and then secrete a vitreous substance, similar to that of the vitreous membrane. Later the two layers of the fold unite to form a retrocorneal tube, and under the cicatricial traction of the cornea partially separate from the posterior surface to form the trabeculae in the anterior chamber.

H F CARRASQUILLO

Experimental Pathology

EFFECT OF CHEMOTHERAPEUTIC AGENTS ON CELL DIVISION AND HEALING OF CORNEAL BURNS AND ABRASIONS IN THE RAT G K SMELSER and V OZANICS, Am J Ophth 27: 1063 (Oct) 1944

Smelzer and Ozanics give the following summary:

"1 Extensive corneal abrasions healed without a marked increase in the number of mitotic figures.

"2 Thermal burns became covered with epithelium in about the same length of time as did abrasions (12-18 hours), but a great increase in the number of mitotic figures was found during this procedure.

"3 Sulfacetamide, sulfapyrazine, and penicillin applied as ointments, powders or solutions had no effect on cell division in the intact rat cornea.

"4 Sulfadiazine tended to increase cell division and sulfathiazole to depress mitosis in this epithelium.

"5 Sulfonamides and penicillin, in general, had no deleterious effect on cell division in abraded corneas, although the number of mitoses was low in over half of the sulfathiazole-treated animals.

"6 Sulfonamides and penicillin did not interfere with cell division in burned corneal epithelium.

"7 Sulfathiazole and sulfacetamide inhibited cell migration following corneal burns, whereas sulfadiazine and penicillin were but slightly detrimental.

"8 Sulfonamide ointments inhibited cell migration slightly less than did powders.

"9 It is realized that these results are qualified by the form of administration and the relative ability of the compounds to penetrate the cornea."

W S REESE

General Pathology

OCULAR PATHOLOGY IN VARIOUS TYPES OF DIETARY DEFICIENCIES, WITH PARTICULAR EMPHASIS ON ARTERIOLAR SCLEROSIS EXPERIMENTAL STUDY A A KNAPP and S N BLACKBERG, U S Nav M Bull 41: 1339 (Sept) 1943

Knapp and Blackberg report that lesions resembling senile arteriosclerosis in man were produced in the eyes of rats with various types

of malnutrition. Faulty nutrition, irrespective of whether the deficiency was caused by inadequate caloric intake or by lack of vitamin A or the vitamin B complex, consistently produced an increased light reflex, pallor and uniform attenuation of the arterioles along their entire course. In previous experiments the authors observed that similar pathologic changes were associated with vitamin D deficiency. The arteriosclerosis induced was not specific for any vitamin deficiency but followed a general, nonspecific disturbance of the cellular nutrition.

J A M A (W ZENTMAYER)

Glaucoma

THE MACULA-WEDGE SCOTOMA A PROGNOSTIC INDEX IN GLAUCOMA J N EVANS, Am J Ophth 27: 1090 (Oct) 1944

After a brief discussion of central field defects associated with glaucoma, Evans describes a new defect which he designates as "macula-wedge" scotoma. It is triangular, and its base arises from the concave border of the sickle defect (scimitar, or Bjerrum defect), and its apex points toward the fixation point.

W S REESE

Hygiene, Sociology, Education and History

INDUSTRIAL EYE HEALTH PROBLEMS H S KUHN, Am J Pub Health 33: 1103 (Sept) 1943

Two problems are of concern to both management and employees—the need of a standard visual test on admission and the use of a similar visual testing procedure in conducting a survey of employees within a given industry. Visual testing falls into three main categories—preemployment examination, periodic rechecks of special groups and the plant survey. Special emphasis on tests for near vision is always indicated when an employee is 40 years and over. The various rehabilitation problems involved in a war program are becoming increasingly important. Among these corrective problems are training of adults who lack coordination of the ocular muscles in development of the needed binocular skills, proper refraction for the distance required by the job and prescription of glasses in relation to that job, detection and care of changes in or disease of an employee's eyes as revealed in the periodic testing, and equipment of each employee so that he is able to meet the visual requirements of his assigned job. Progress in the field of industrial ophthalmology, in eye protection equipment, in the analysis of visual aptitudes, in the classification of jobs as related to visual skills and, especially, in the unexpected responsibilities of ocular rehabilitation in a country at war has been so rapid that constant reference to current scientific literature is indicated.

W ZENTMAYER

Injuries

PNEUMO-ENCEPHALOCELE, SECONDARY TO A PUNCTURE WOUND OF THE LID H SLAUGHTER and B Y ALVIS, Am J Ophth 27: 617 (June) 1944

The case of a child who presumably injured her lid with a pencil is described. Pus was obtained when the lid was incised, culture of which showed *Staphylococcus aureus*. A diagnosis of traumatic pneumoencephalocele was made on the basis of the roentgenogram. The child recovered.

W S REESE.

ACTINIC KERATOCONJUNCTIVITIS R G SCOBEE and E W GRIFFEY, Am J Ophth 27: 632 (June) 1944

Scobee and Griffey conclude that actinic keratoconjunctivitis, or "flash burn," is an important industrial disease and that the causative agent is ultraviolet irradiation. Epinephrine used early greatly reduces the severity, or even aborts the condition entirely.

W S REESE

SOVIET MILITARY OPHTHALMOLOGY A A KOLEN, Lancet 1: 804-805 (June 26) 1943

Soviet ophthalmologists have paid a great deal of attention to the study of war injuries of the eyes, and the military ophthalmic services are so equipped as to insure the earliest possible skilled attention to the wounded eyes. This article speaks of the following plastic procedures: reconstruction of the conjunctival sac, correction of contracted scars and reconstruction of an eyelid by the flap method of Kurloff. Plastic operations are performed within two to four months after the injury, so as to facilitate early rehabilitation of the patient. To facilitate the disappearance of unsightly scars, paraffin therapy is practiced. In cases of prolapse of the ciliary body associated with scleral rupture of the eyeball the Soviet surgeons do not hesitate to excise the prolapsed ciliary body and then unite the scleral wound with sutures; in fact, they speak of surgery of the ciliary body.

Transfusions are widely used in the treatment of ocular wounds. They are regarded as especially useful in cases of traumatic opacities of the vitreous, traumatic iridocyclitis and threatened sympathetic ophthalmia. In an injury of the ciliary body a prophylactic transfusion of 150 to 200 cc of blood is made. Absorption of the opacities in the vitreous has been facilitated by transfusion into the duodenum by means of the duodenal probe of between 50 and 120 cc of duodenal juice. Blood transfusion is combined with paracentesis of the anterior chamber in cases of severe and persistent vitreous opacities. With infected injuries of the eyeball excellent results have been achieved by the administration of

sulfacetamide, and the advantages of vitamin K in prevention of threatened hemorrhages are mentioned.

This brief and somewhat optimistic article will be found stimulating and suggestive.

ARNOLD KNAPP

Lacrimal Apparatus

THE LACRIMATION REFLEX J R. MUTCHE, Brit Ophth 28: 318 (July) 1944

Mutch, in this lengthy article, considers the lacrimation reflex under the headings of physiology, nerve supply, experimental observations, clinical observations and conclusions. He draws the following conclusions:

Reflex lacrimation is unilateral and can be inhibited by surface anesthesia of the conjunctiva and cornea and by section or paralysis of the ophthalmic division of the fifth cranial nerve. This nerve is therefore the sensory, or afferent, pathway for reflex lacrimation.

The efferent pathway runs in the seventh cranial nerve but is independent of the motor fibers to the facial muscles (syndrome of crocodile tears) and of the seventh nerve in the brain near the nucleus of the sixth nerve (Foville's syndrome, or lateral gaze paralysis) and is also peripheral to the geniculate ganglion (Bell's palsy, with loss of taste on the anterior two thirds of the tongue).

If the greater superficial petrosal nerve is cut or the sphenopalatine ganglion is blocked, no reflex or psychic lacrimation takes place, even though the ophthalmic division of the fifth nerve is left intact, while psychic lacrimation is normal if the sensory root of the fifth nerve is cut and the greater superficial petrosal nerve is spared. Motor impulses must therefore pass along the greater superficial petrosal nerve.

Psychic weeping is bilateral and cannot be inhibited by surface anesthesia or paralysis of the fifth cranial nerve or by section of the cervical sympathetic nerve.

On anatomic grounds, it is assumed that the fibers from the sphenopalatine ganglion which enter the maxillary nerve run to the trigeminal (gasserian) ganglion before they pass along the zygomatic nerve.

No interference with reflex or psychic lacrimation results from either unilateral or bilateral section of the cervical sympathetic chain in the neck. One patient did complain that her eyes felt unduly dry toward night, so there is a possibility that mucus from the glands in the conjunctiva may be inhibited. On no occasion, however, has keratitis sicca been observed in any patient who has had a sympathectomy. It is unlikely, therefore, that the sympathetic nerve takes any part in reflex or psychic lacrimation.

W ZENTMAYER

Lens

A REPORT ON A FAMILY WITH ECTOPIC LENSES
C A CLAPP, Am J Ophth 27: 738 (July)
1944

Clapp reports on 11 children in one family of whom 8 have misplaced lenses and a ninth has congenital cataract

W S REESE

CORNEAL SUTURES IN CATARACT OPERATION
L E MARTÍNEZ, Arch Asoc para evit
ceguera México 1 155, 1942

The author states that although good results have been obtained with the classic cataract operation in a large percentage of cases since Daviel's time, the use of sutures to avoid postoperative complications has become established. Sutures are most useful in intracapsular extraction, with which loss of vitreous is more likely to occur.

The following types of suture are used conjunctivocorneal, corneoscleral intacorneoscleral and suture by layers. The first type has been described by Arganaraz of Buenos Aires. As an example of the corneoscleral type, the author cites the suture devised by Liégard, modifications of which have been described by Olmos, Chavira and Tores Estrada. The suture described by Suárez de Mendoza is of the intacorneoscleral type, and Castroviejo employs suture by layers.

The author explains the procedure employed with each type of suture. He is of the opinion that the use of sutures is an advance in ophthalmology and states that even if all complications cannot be avoided, they should nevertheless be employed systematically.

H F CARRASQUILLO

Methods of Examination

OCULAR BIOPHOTOMICROGRAPHY PRELIMINARY
REPORT M DE RIVAS CHERIF, Arch Asoc
para evit ceguera Mexico 1-119, 1942

It is the author's belief, although he has not yet reviewed the literature, that attempts must have been made to obtain photomicrographs of the living eye, but with no practical results, since he has never seen such pictures in publications of any kind. He has succeeded in obtaining biophotomicrographs of the eye, which, although not perfect at present, he hopes to improve on so that they will be of practical value.

He employs a camera obscura without an objective of its own, utilizing the oculars of the biomicroscope. As the corneal microscope is binocular, he uses one of the oculars for observation and the other for photography. He describes and illustrates the simple apparatus which he employs in the experimental work and shows some of the photographs obtained.

H F CARRASQUILLO

Neurology

A DIFFUSE NEUROFIBROMATOSIS OF THE BULBAR CONJUNCTIVA (RECKLINGHAUSEN'S DISEASE), WITH LESIONS OF THE OSSEOUS SYSTEM AND OF THE SKIN, BODILY ASYMMETRY AND INTRACRANIAL DISTURBANCES REPORT OF A CASE F P ALLENDE, Arch de oftal de Buenos Aires 18: 438 (Sept) 1943

The author discusses Recklinghausen's disease. He establishes three clinical groups: cases in which the invasion of the central nervous system is predominant, cases in which the cutaneous lesions are the principal manifestation of the disease, and cases in which involvement of the skeletal system is predominant.

When the structures of the eye are involved, the order of preference is as follows: first the lids and optic nerve, then the orbit, retina, choroid, iris, cornea and tarsal conjunctiva, and, last, the bulbar conjunctiva. The author describes the different types of lesions in these locations and stresses the rarity of involvement of the bulbar conjunctiva. He refers to the fact that Duke-Eldei mentions only 2 cases so far described, that after careful search of the literature he himself found reports of only 3 cases and that from 1932 to 1942 articles containing only 34 cases of the disease with ocular complications are listed in the *Quarterly Cumulative Index Medicus*.

He reports a case with involvement of the bulbar conjunctiva in a girl aged 18. General physical examination showed developmental asymmetry of the body, with predominance of the right side, two large patches of baldness over the right temporoparietal region, with a solid tumor, the size of a hazelnut, in the temporal region, and typical café au lait macular lesions of the skin. Neurologic examination revealed that the patient was epileptic, and a psychiatric study demonstrated that she was mentally retarded when going to school.

Right Eye.—Examination revealed hyperplasia of the surface of the skin adjacent to the temporal region, cranio-orbital asymmetry, a pinkish, hair-free tumor in the superciliary region, a smaller growth over the anterior surface of the upper lid, blepharoptosis, hypertrophy of the palpebral portion of the lacrimal gland, a flat, round tumor in the bulbar conjunctiva near the limbus at 3 o'clock, a small tumor in the caruncle, and a larger tumor in the bulbar conjunctiva, above the cornea and slightly invading it, which measured 2 cm in its widest dimension. Examination of the fundus revealed the presence of a fine, epipapillary membrane. The rest of the fundus was normal. Vision was 1/6 and was not improved by glasses or pinhole disk.

The left eye was normal.

Laboratory examination revealed essentially nothing abnormal. Roentgenographic studies con-

firmly the cranio-orbital and bodily asymmetry. Biopsy confirmed the diagnosis of neurofibromatosis.

The article is well illustrated with photographs and photomicrographs.

H F CARRASQUILLO

Ocular Muscles

PHENOMENA ASSOCIATED WITH ECCENTRIC FIXATION G GUIBOR, Am J Ophth 27: 986 (Sept) 1944

Guibor gives the following summary:

"The phenomena associated with eccentric fixation when studied intensively may be summarized under three headings: 1 Disturbances associated with the motor apparatus; 2 Disturbances associated with the visual apparatus; 3 Disturbances associated with the proprioceptive apparatus."

"Disturbances associated with the motor apparatus may be said to be: 1 The esotropia; 2 The limitation of abduction (weakness in the left external rectus muscle). Induced homonymous diplopia which increased in the field of the left external rectus muscle; 3 Abnormal electroencephalogram."

"Disturbances associated with the visual apparatus may be outlined as: 1 Amblyopia (3/200-3/140); 2 A central scotoma; 3 Normal peripheral field; 4 Normal projection; 5 Abnormal correspondence."

"Disturbances associated with the proprioceptive apparatus may be said to be illustrated by: 1 Head rotation; 2 Past pointing; 3 Past walking."

"Note: Authorities do not agree that a proprioceptive apparatus is present in the extraocular-motor mechanism. Clinical evidence suggests that such a mechanism does exist."

W S REESE

Pharmacology

REACTIVITY OF THE OCULAR TISSUES TO WETTING AGENTS K C SWAN, Am J Ophth 27: 1118 (Oct) 1944

Swan points out that although the low toxicity of wetting agents has been stressed in the literature and in commercial advertisements, these surface-active compounds are capable of producing reactions in ocular tissues, indeed, minute amounts injected into the anterior chamber produce violent reactions.

W S REESE

SOME NEW CHOLINE ESTERS WITH CYCLOPLEGIC AND MYDRIATIC ACTION K C SWAN and N G WHITE, Proc Soc Exper Biol & Med 53: 164 (June) 1943

Choline derivatives, such as acetylcholine and carbaminoylecholine, are miotics and cycloplegics. The authors have synthesized new choline esters

by substituting highly hydrophobic groups for the acetyl radical in acetylcholine. The resulting elongated molecules have proved highly surface active, in sharp contrast to the surface-inactive acetylcholine. Of the new compounds, di-n-butylcarbaminoylecholine sulfate has been found to be a powerful mydriatic and cycloplegic. Two instillations of a 7.5 per cent solution of the compound into the conjunctival sac of an adult patient produce mydriasis and cycloplegia, beginning within twenty minutes and becoming maximal in sixty to ninety minutes. The reactions of the intrinsic muscles usually return to normal seven to twelve hours after administration. Four hundred patients received two instillations of 5 per cent homatropine hydrobromide in one eye and two instillations of a 7.5 per cent solution of the new drug in the other. There was little difference in the degree of mydriasis and cycloplegia produced by the two drugs, however, cycloplegia, and particularly mydriasis, was shorter after the administration of the new drug. Synthesis and pharmacologic investigation of surface-active choline esters are being continued.

KRONFELD

Refraction and Accommodation

BIASTIGMATISM A LINKSZ and W TRILLER, Am J Ophth 27: 992 (Sept) 1944

Links and Triller conclude from their studies that since the Méiquez procedure cannot furnish more accurate results than the direct use of the astigmatic dial there is nothing that would recommend the adoption of this complicated technic for routine refractive examinations.

W S REESE

THE GAS MASK WATER FOR PRESBYOPIA W O G TAYLOR, Brit J Ophth 28: 461 (Sept) 1944

Taylor describes a method of correction of presbyopia for use on respirators with or without additional correction for ametropia. The optical problems are considered. The device has the advantage of cheapness, lightness, absence of mechanical parts, freedom from dimming and ease of testing and fitting. The article is illustrated.

W ZENTMAYER

Retina and Optic Nerve

ARTERIOLAR THROMBOSIS OF THE RETINA C S DANIEL and M BRODSKY, Arch de oftal de Buenos Aires 18: 429 (Sept) 1943

The authors report the case of an athlete aged 33 who had been alcoholic all his life. The Wassermann and Kahn reactions of the blood were negative. One month before the visual symptoms appeared he began to lose weight and strength, and ten days after this he had a cerebral episode, with loss of consciousness for eight

hours Twenty days later he complained of blurred vision in the right eye

Visual acuity was 4/10 in the right eye and 8/10 in the left eye External examination revealed nothing abnormal in either eye, and the ophthalmoscopic findings in the left eye were normal In the right eye there were arteriosclerotic changes in the inferior macular artery, a branch of which was completely obliterated with a resulting edematous area having an elevation of 4 D in the region of the macula Numerous white dots were also seen in this zone

Study of the fields in this eye demonstrated a triangular sector defect, limited by a straight line continuous with a scotoma surrounding the central area, which was free Eight months later vision in the right eye was 8/10, and the edematous area at the macula was attenuated The visual field remained unchanged

The authors differentiate the condition from embolism, endarteritis and thrombosis, toxic and diffused periarteritis and local ischemic states brought about by orbital conditions, the result of traumatism, pressure and inflammatory processes They state that their case falls into the category of the condition described by Friedenwald as "retinal arteriolar thrombosis"

The article is illustrated

H F CARRASQUILLO

Tumors

OCULAR COMPLICATIONS OF TUMORS OF THE NASOPHARYNX B J TISCORNIA and I LAMI, Arch de oftal de Buenos Aires 18: 557 (Nov) 1943

Little has been written in ophthalmologic literature on this subject, although the condition frequently produces initial ocular symptoms

After the authors describe the intranasal and extranasal symptoms of the disorder, they mention the following ocular manifestations muscular palsies, enophthalmos, neuralgias, ptosis, exophthalmos, edema and atrophy of the optic nerve, which, according to many observers, are common in the disease

The anatomy of the nasopharynx and the surrounding region is described in detail, and how involvement of the different nerve structures is responsible for the ocular manifestations The extension to the external rectus muscle occurs early at times, and paralytic convergent squint is the result The third nerve is usually invaded late in the disease, producing external or internal ophthalmoplegia The optic nerve may be involved, and papilledema or atrophy may occur

Involvement of the gasserian ganglion may result in severe neuralgia Horner's syndrome may occur from involvement of the ciliospinal center or the cervical sympathetic outflow, and unilateral miosis, ptosis, ocular hypotony, exophthalmos and congestion of the skin of the side of the face may be noted

Exophthalmos is frequent and is the result of invasion of the orbit by the tumor Abnormality in the lacrimal secretion may be produced by involvement of the secretory branches of the facial nerve

The most common tumors involving the nasopharynx are the epitheliomas and the sarcomas Observations in 8 clinical cases are given

H F CARRASQUILLO

Uvea

A CASE OF CORPORA NIGRA WITH ANTERIOR SYNECHIA R CRAWFORD, Brit J Ophth 28: 410 (Aug) 1944

The especial feature of the case was the attachment of one of the upper corpora nigra in the left eye to the back of the cornea over a flattened area of about 2 mm The position and size remained constant whether the pupil was normal or dilated It is suggested that one of the flocculi passed through the pupillary membrane about the fifth month of fetal life, when the marginal sinus is well developed and the anterior chamber is still shallow, and became adherent to the cornea

W ZENTMAYER

Vision

THE DISSOCIATION OF FORM VISION AND LIGHT PERCEPTION IN STRABISMIC AMBLYOPIA G WALD and H M BURIAN, Am J Ophth 27: 950 (Sept) 1944

Wald and Burian give the following summary

"1 The absolute threshold of vision has been measured under various circumstances in five patients with strabismic amblyopia In all cases thresholds were determined alternately in the amblyopic and dominant eyes Three types of measurement were performed (*a*) dark adaptation following a high state of light adaptation, (*b*) the distribution of thresholds over the retinal surface, central and peripheral, in the dark-adapted eye, and (*c*) the variation of threshold with wave length, centrally and peripherally, in the dark-adapted eye

"2 In all cases the threshold of the amblyopic eye was found to be essentially normal, foveally and peripherally, in cones and rods, and in light and dark adaptation With this is associated a capacity approaching normal for fixating and localizing illuminated points and areas on the central and peripheral retina

"3 The entire apparatus of simple light perception and spatial localization within the visual field is therefore virtually normal in these patients Since, however, the visual acuities of their amblyopic eyes were in no case higher than 20/200, the apparatus of pattern vision must be to some degree distinct from that which mediates the other visual functions

"4 Subhuman mammals which have been deprived of the occipital lobes of the cerebral cortex, which contain the visual areas, also lose virtually all capacity for pattern vision while retaining sensitivity to light, brightness discrimination, and visual-space localization. Pattern vision in mammals generally, therefore, requires the cortex, while other visual functions appear to be in large measure subcortical. In man there is evidence that all sensory aspects of vision have indispensable cortical components. Our experiments, however, show that here also some degree of anatomic dissociation of visual functions must exist.

"5 In view of these relationships, and of the demonstrated effectiveness of use and training in curing some cases of strabismic amblyopia, it is concluded that this disability consists in a cortical inhibition of the higher cortical function of pattern vision without notable impairment of the lower cortical functions of light perception and spatial projection.

"6 The possibility exists that this inhibition involves principally the macular projection on the cortex and, perhaps as a consequence of this, pattern vision primarily in bright light."

W S REESE

NIGHT BLINDNESS OF WAR P H WOSIKA,
War Med 4: 331 (Sept) 1943

According to Wosika, night blindness of war was first reported during the Crusades, and since that time almost all major military efforts have been accompanied with night blindness, particularly wherever overstraining, heat, sun blinding, hunger and thirst have occurred. The First World War was responsible for much literature on this subject. The term "night blindness of war" embraces organic and idiopathic night blindness. In the literature poor dark adaptation, as measured by instruments, also has been included under this term. Malnutrition (lack of vitamin A) causes night blindness, xerosis and xerophthalmia. Therapeutic correction is simple, swift and sure. Poor dark adaptation does not seem related to night blindness, xerosis, xerophthalmia or food inadequacy. Therapeutic correction is not successful, even with huge supplemental doses of vitamin A. In the present state of knowledge of scotopic vision, night blindness and poor adaptation must be differentiated. It is suggested that further work with the rate and end values of dark adaptation concerning rods, cones and influences

of the nervous system be performed in an attempt to establish a firm physiologic basis for dark adaptation tests. While dark adaptation tests do measure the ability to see in low luminosity, the controlling mechanism is not established, the relation to vitamin A is not clear, and its usefulness in military medicine as regards night blindness of war must be questioned, although further refinements of technic may enhance the value of the test.

J A M A (W ZENTMAYER)

Therapeutics

VITAMINS IN OPHTHALMOLOGY. I BILGER,
Goz klin 1: 43, 1943.

The author states that when one surveys the advances made in the study of nutrition up to the present, one is impressed with the importance of the vitamins. With respect to the ocular disorders, the absence of vitamin A causes day blindness, xerophthalmia and keratomalacia and secondarily is concerned with lesions of the cornea, lids and conjunctiva and with strabismus.

W ZENTMAYER

News and Notes

EDITED BY W L BENEDICT

GENERAL NEWS

Ophthalmologic Seminar, Emory University School of Medicine—The ophthalmologic seminar announced by Emory University School of Medicine has been postponed on advice from the War Committee on Conventions.

American Orthoptic Council: Examinations for Technicians—The next examination by the American Orthoptic Council will be held in September and October 1945.

The written examinations will be held at various cities in the country on Friday, September 7. Only candidates passing the written examinations will be permitted to take the oral and practical tests, to be given in Chicago, Saturday, October 6.

Applications on official forms must be received before July 1, 1945.

Address The American Orthoptic Council, 23 East Seventy-Ninth Street, New York 21

Society Transactions

EDITED BY DR W L BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H JOHNSON, M D, *Chairman*
AND
WENDELL L HUGHES, M D *Secretary*
Regular Meeting, Nov 20 1944

Choroideremia Report of a Case DR HARRY MAGDER, Kirkland Lake, Ontario, Canada (by invitation)

A case of choroideremia in a man aged 58 is presented. The patient was only slightly myopic, whereas most patients reported on have shown a moderate or high degree of myopia.

The disease had been progressive for over ten years so that a change from night work to day work was necessary three years ago. The fundus picture and field defects were practically identical in the two eyes. Central visual acuity has remained fairly good, despite the advanced condition of the disease.

DISCUSSION

DR W GUERNSEY FREY In the twenty-two years during which I have been associated with various eye and ear hospitals in Brooklyn, Queens and Manhattan, this is the first case of choroideremia I have knowingly encountered. The only diagnosis with which this condition might be confused is retinitis pigmentosa and the resemblance there is only with respect to night blindness, not appearance.

DR JOSEPH ANTHONY SCHULTZ, Buffalo
Were any choroidal vessels at all observed?

DR HARRY MAGDER Kirkland Lakes, Ontario, Canada Yes in the periphery of each eye considerable choroidal tissue was to be seen, with the vessels as well.

Ophthalmic Features of Intracranial Chordoma and Allied Tumors of the Clivus DR ISADORE GIVNER

This paper will be published in full in a future issue of the ARCHIVES

Effect of Local Anesthetics on Healing of Burns of the Cornea DR G K SMELSER

The effects of local anesthetics on two major factors in the healing of epithelial injuries, mitosis and migration of the cells, are compared. Seven anesthetics (cocaine 0.5 per cent, tetracaine hydrochloride, 0.5 0.25 and 0.1 per cent, phenacaine hydrochloride, 2 and 0.5 per cent, butacaine sulfate 2 and 0.5 per cent, butesin picrate 0.75 and 2 per cent, and orthoform, 2 per cent) were studied. These concentrations

are those which are clinically useful. These compounds were applied as aqueous solutions, or as ointments or as both. An ointment base and an aqueous solution of hydrogen ion concentration similar to that of the anesthetic solutions were tested in like manner.

Young male rats of the Sherman strain were used. Standard thermal burns were made on each eye with a special Shahan thermophore, as described in earlier reports. Untreated burns were covered with epithelium in twelve to fifteen hours. The control series showed that the speed of migration and the number of mitotic figures were essentially the same in the two eyes. The substances to be tested were placed on the right eye for one minute every two hours. Autopsy was performed on the animal twelve hours after the injury, and the eyes were fixed. Camera lucida drawings were made of the portion of the burn which remained uncovered by epithelium, and the area thus outlined was measured with a planimeter. Counts of the mitotic figures in the regenerating epithelium were made from paraffin sections. The effect of the anesthetic was judged by comparing the treated eye with the untreated, control, left eye of the same animal.

The effect of these anesthetics on mitosis in the intact cornea is reported. When the same drug at the same concentration is applied to an injured eye its inhibitory effect on cell division is often greater than in the intact eye. This is due, perhaps, to the greater ability of the drug to enter broken epithelium. In these experiments all the anesthetics checked cell division appreciably except for phenacaine hydrochloride, 0.5 per cent, and butesin picrate 0.75 per cent. The form in which the drug was administered was also important, for an ointment containing butacaine sulfate in 2 per cent concentration was much less inhibitory than the same drug in a 2 per cent solution.

All substances tested retarded migration of the epithelial cells over the burned area. A control solution (boric acid, p_{H} 4.0) and anhydrous wool fat, the ointment base slightly inhibited cell migration. Solutions of nupercaine hydrochloride, 0.25 per cent, butacaine sulfate, 2 per cent, and tetracaine hydrochloride, 0.5 per cent, and phenacaine hydrochloride, 2 per cent, notably restricted cell movement. Some of the anesthetics actually enlarged the denuded area, possibly because of their detergent qualities. However, certain anesthetics in low concentrations are relatively harmless to regenerating epithelium. Solutions of phenacaine hydrochloride, 0.5 per cent, or cocaine, 0.5 per cent and ointments contain-

ing butacaine sulfate, 2 per cent, or butesin picrate, 0.75 per cent, did not notably delay healing as compared with an ointment with an anhydrous wool fat base or a 3 per cent solution of boric acid

DISCUSSION

DR CHARLES ALLEN PERERA I should like to ask Dr Smelser whether there is any way to differentiate between the local chemical effect of the anesthetic on the epithelium and the trophic effect of anesthesia of the corneal nerves on the growth of epithelium, and whether there would be any point in carrying out another series of experiments in which anesthesia is obtained not by local use but by injection behind the globe

QUESTION FROM AUDIENCE Has Dr Smelser studied the effect of metycaine on the cornea and the effect of various anesthetics when combined with other drugs used in treatment of the cornea, for example, 5 per cent sulfathiazole is frequently used in conjunction with the anesthetic

DR BEAUMONT, New Zealand I should like to ask Dr Smelser what the effect of sodium bicarbonate would be

DR G K SMELSER I do not know that I can answer Dr Perera's question. I studied only the direct effect of these anesthetics on the cells, whether they act directly on the metabolism of these cells through their action on the nerve. I do not know. That would be an interesting investigation. One can produce anesthesia by methods other than the application of these local anesthetics, and, so far as I am aware, they act in the same manner, that is, they retard cell division. However, the anesthesia itself does not necessarily inhibit the migration of epithelium. My co-workers and I have injected anesthetics subconjunctivally and have produced anesthesia by intraperitoneal injection, and the latter type of treatment does not inhibit cell migration or cell division, so far as we have studied it. The time required to complete a mitotic division may be affected. I have not done any experiments on the effect of the retrolbulbar injection of drugs. Subconjunctival injection of cocaine or procaine or procaine combined with epinephrine was harmful to mitosis.

I have not done any experiments on the effect of bicarbonates.

I have not had any experience with metycaine. We have carried out experiments with the sulfonamide compounds, in exactly the same manner. We have studied their influence on both corneal burns and abrasions. Sulfathiazole by itself definitely inhibits mitosis and the migration of epithelium. We have also carried out experiments with sulfadiazine, which did not decrease cell division and when employed in ointment form or as fine crystals is not harmful. The corneal cells divide readily in the presence of sulfacetamide, but this drug inhibits cell migration. Penicillin is not at all harmful. The results of these experi-

ments have been published in the *American Journal of Ophthalmology* (27: 1063 [Oct] 1944)

Thrombosis of the Central Vein Treated with Heparin DR R TOWNLEY PATON

Heparin may be considered a rather harmless anticoagulant when properly administered.

The prognosis in cases of complete thrombosis of the central vein treated with heparin may still be considered as practically hopeless. In 4 out of 5 cases in which adequate treatment with the drug was carried out was finally necessary. In 10 cases of partial thrombosis of the central retinal vein treatment with heparin gave encouraging, but not dramatic, results.

No patient with recent thrombosis of the retinal vein should be denied the administration of heparin, unless study of a much larger series of cases proves it to be of doubtful value.

Regular Meeting, Dec 18, 1944

A New Hemispheric Perimeter DR ARTHUR MINSKY

A new instrument is presented and described which will enable the ophthalmologist to plot diplopia fields accurately, to test tropias, to determine peripheral fields, to plot detachments, to locate retinal tears and to prove the presence or absence of central color scotoma. A calibrated right angle dioptric scale enables him to evaluate the displacement of the plotted points without the use of prisms.

The instrument is a transparent, plastic hemisphere with a radius of 310 mm, stamped by degrees in the eight principal meridians. These markings are inconspicuous to the patient. Notations can be made on the hemisphere with temporary markings and the findings transferred to permanent records.

This perimeter has the following advantages. Measurements for tropias and diplopias are made at a constant fixed radius and in a constant meridian, the patient is oriented in space, the patient is under constant observation, the examination can be made rapidly, the instrument is portable and readily used in bedside examination, it has no moving parts or adjustable arm, and it is relatively inexpensive.

DISCUSSION

DR THOMAS H JOHNSON This is an ingenious perimeter, and, so far as I know, this plastic arrangement is entirely new.

DR WENDELL L HUGHES, Hempstead, N Y I should like to speak first about the background, which Dr Minsky has not said much about.

On account of the uncontrolled background, visibility of a test object might vary in different portions of the field. One might be testing with a white object against a dull gray wall, where it might show up well in contrast, and if the object were moved farther up, it would show up very

poorly by contrast against a white ceiling. If the object were placed on a meridian so that it came in front of the examiner's dark coat during part of its excursion and against a light background in another part, variable results would be obtained. I wonder whether Dr Minsky has made any provision for the lighting on the face of the test object. Is the illumination on the face of the object controlled? I think the idea is an ingenious one and will bear greater development.

DR THOMAS H JOHNSON Di Wheeler, how do you think this instrument will compare with the tangent screen for the plotting of diplopia?

DR MAYNARD C WHEELER It should be a convenient way to plot diplopia. I am sorry that Dr Minsky has become tired of holding up prisms, for I do not think that his perimeter will replace them.

DR ARTHUR MINSKY We have not done any work on the background. I have used a light green wall, and it has worked rather effectively. Di Hughes's point about lighting is a good one, and I shall try to do something about it.

DR THOMAS H JOHNSON Who will manufacture this perimeter?

DR ARTHUR MINSKY I do not know. I have been working on a plastic hemisphere for two years and could not obtain one which had the same thickness throughout until one of my friends got it for me. The perimeter will probably not be available for civilian use until the end of the war.

Test for Liability of Ocular Tension

DR ROBERT K LAMBERT and DR SYLVAN BLOOMFIELD

This paper will appear in full in a future issue of the ARCHIVES.

Iridencleisis for Glaucoma DR ALGERNON B REESE

This paper will appear in a future issue of the ARCHIVES.

Method for Extraction of Subluxated Lenses

DR G BONACCOLTO

The method was presented accompanied with six colored slides portraying the main steps of the operation. Three moving pictures in color, representing 3 cases of dislocated lens, were shown.

The operation is preceded by lid sutures, substituted for the speculum, retrobulbar injection and suture of the superior rectus muscle. A conjunctival incision is made 2 mm above the limbus and carried concentrically with it. Three double-armed silk sutures are passed 2 mm from the limbus at 10, 12 and 2 o'clock. A keratome incision, at the superior limbus, is completed with scissors. The arms of the superior sutures are placed through the con-

junctiva attached to the cornea. The conjunctival flap is firmly held with fine forceps, while the cataract loop is introduced into the vitreous and passed quickly behind the lens, pushing it against the cornea. This is done with a quick traction movement. The lens is expelled from the anterior chamber. The superior suture is gently tied, after which the auxiliary sutures are passed and tied. Seven patients were operated on with successful results.

DISCUSSION

DR DAVID H WEBSTER This procedure is a distinct contribution to ophthalmology. I have seen Dr Bonaccolto's results, and they are satisfactory. As long as the lens is visible while the patient is in a supine position, this technic is ideal, but the cases which present serious difficulties are those in which the lens floats freely in the vitreous and appears in the lower section of the vitreous when the patient is in an erect position, appears in the pupillary area or in the anterior chamber when the patient is in a prone position and drops back into the vitreous the moment the patient is turned in a supine position. I do not know whether it has been Dr Bonaccolto's unfortunate experience to have to encounter such a case. Verhoeff, when this happened after he made his section, and the lens disappeared into the vitreous, directed his assistant to pour a stream of saline solution into the anterior chamber until the lens appeared where he could loup it out. On several occasions Dr David Webster Sr turned the patient in a prone position, transfixed the lens by passing a knife needle, which entered the globe 8 mm behind the limbus, and then turned the patient over in a supine position and completed the operation. I myself have operated in 2 such cases, in each instance assisted by the late Dr H R Skeel. We placed the patient in a prone position, and we sat on the floor, made our incision and removed the lens, with slight loss of vitreous, in each instance the patient had 20/30 vision. Perhaps I am too old to try that now, but I believe it would be my operation of choice. I should like to know what Dr Bonaccolto would do in a case in which he has a lens floating free in the vitreous.

DR WENDELL L HUGHES, Hempstead, N Y In answer to Dr Webster's question, the Hague lamp will render the lens brilliantly visible, so that it is illuminated the moment its edge is pushed into the pupil with the lens loop in the vitreous, then one can easily get the loop behind it because its location is so readily made out with good ultraviolet light.

DR G BONACCOLTO I was going to suggest exactly what Dr Hughes mentioned. With this light one can see the lens, and once it has been located it can be rather simply and safely extracted from the vitreous with the method I have just described.

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Place University Club, Salt Lake City Time 7 00 p m, third Monday of each month

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Time First Monday in January, March, May and November

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Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m, fourth Thursday of each month from October to March

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Secretary Dr Luther E Wilson, 919 Woodward Bldg, Birmingham, Ala
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Secretary-Treasurer Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn 16
Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

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Time Second Thursday of each month

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Place Mountain City Club Time Second Thursday of each month from September to May

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Secretary Dr W A Mann, 30 N Michigan Ave, Chicago 2
Place Continental Hotel, 505 N Michigan Ave
Time Third Monday of each month from October to May

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Secretary Dr A A Levin, 441 Vine St, Cincinnati
Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

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Secretary Dr Carl Ellenberger, 14805 Detroit Ave, Cleveland
Time Second Tuesday in October, December, February and April

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Clerk Dr George F J Kelly, 37 S 20th St, Philadelphia
Time Third Thursday of every month from October to April, inclusive

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LARYNGOLOGICAL SOCIETY**

Chairman Dr Erwin W Troutman, 21 E State St, Columbus, Ohio
Secretary-Treasurer Dr T Rees Williams, 380 E Town St, Columbus 15, Ohio
Place University Club Time 6 15 p m, first Monday of each month, from October to May, inclusive

**CORPUS CHRISTI EYE, EAR, NOSE AND
THROAT SOCIETY**

Chairman Dr C B Collins, 704 Medical Professional Bldg, Corpus Christi, Texas
Secretary Dr L W O Janssen, 710 Medical Professional Bldg, Corpus Christi, Texas
Time 6 30 p m, third Tuesday of each month from October to May

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OTO-LARYNGOLOGY**

President Dr Ruby K Daniel, Medical Arts Bldg, Dallas 1, Texas
Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1, Texas
Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month from October to June The November, January and March meetings are devoted to clinical work

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President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa
 Time 7 45 p m, third Monday of every month from September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically
 Secretary Dr Cecil W Lepard, 1025 David Whitney Bldg, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time First Wednesday of each month, November to April, inclusive

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Raymond S Gouy, 545 David Whitney Bldg, Detroit 26
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Appointed at each meeting
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany
 Time Third Wednesday in October, November, March, April, May and June

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

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President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Dennis Smith, 623 Security Bldg, Long Beach 2, Calif
 Secretary-Treasurer Dr Robert Null, 710 Security Bldg, Long Beach 2, Calif
 Place Seaside Hospital Time Last Wednesday of each month from October to May

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif
 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order
 Secretary Dr James J Monahan, 31 S Jardin St, Shenandoah, Pa

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Chairman Dr P S Constantinople, 1835 I St N W, Washington
 Secretary Dr Frazier Williams, 1801 I St N W, Washington
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Leon H Guerin, 324 E Wisconsin Ave, Milwaukee 2
 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2
 Place University Club Time 6 30 p m, fourth Tuesday of each month from October to May

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio
 Secretary-Treasurer Dr Martland D Place, 981 Reibold Bldg, Dayton, Ohio
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada
 Time Second Thursday of October, December, February and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

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Chairman Dr Thomas H Johnson, 30 W 59th St, New York
 Secretary Dr Wendell L. Hughes, 131 Fulton Ave, Hempstead, N Y
 Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Milton Berliner, 57 W 57th St, New York
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City
 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City
 Place University Hospital Time Second Tuesday of each month from September to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr. D D Stonecypher, Nebraska City, Neb
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia
 Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia
 Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr George H Shuman, 351-5th Ave, Pittsburgh
 Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Michael J Penta, 312 N 5th St, Reading, Pa
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

RICHMOND OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va
 Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis
 Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis
 Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except December

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas
 Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine, Randolph Field, Texas
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center
 Time 7 p m, second Tuesday of each month from October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco
 Secretary Dr A G Rawlins, 384 Post St, San Francisco
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W Riverside Ave, Spokane, Wash
 Secretary Dr Clarence A Veasey Jr, 421 W Riverside Ave, Spokane, Wash
 Place Spokane Medical Library Time 8 p m, fourth Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St, Syracuse, N Y
 Secretary-Treasurer Dr I H Blaisdell, 713 E Genesee St, Syracuse, N Y
 Place University Club Time First Tuesday of each month except June, July and August

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr L C Ravin, 316 Michigan St, Toledo 2, Ohio
 Secretary Dr W W Randolph, 1838 Parkwood Ave, Toledo, Ohio
 Place Toledo Club Time Each month except June, July and August

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr W R F Luke, 316 Medical Arts Bldg, Toronto, Canada
 Secretary Dr W T Gratton, 216 Medical Arts Bldg, Toronto, Canada
 Place Academy of Medicine, 13 Queens Park Time First Monday of each month, November to April

WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr Harold M Downey, 1740 M St N W, Washington, D C
 Secretary-Treasurer Dr Richard W Wilkinson, 1408 L St N W, Washington, D C
 Place Medical Society of District of Columbia Bldg, 1718 M St N W, Washington, D C Time 7 30 p m, first Monday in November, January, March and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn
 Secretary Dr Samuel T Buckman, 70 S Franklin St, Wilkes-Barre, Pa
 Place Office of chairman Time Last Tuesday of each month from October to May

CORRECTION

In the article by Major John G Bellows entitled "The Crystalline Lens in Diabetes Mellitus," in the December 1944 issue (ARCH OPHTH 32:498-507), the statement on page 502, line 12, first column, "and later by Ascher" is incorrect. The reference to Dr Ascher was concerned with an article on intraocular pressure in diabetic patients, and in that work no opinion was expressed that the lens was poisoned by a high concentration of dextrose.

CHOICE OF OPERATION FOR PRIMARY GLAUCOMA COMBINED WITH CATARACT

JACK S GUYTON, MD

BALTIMORE

Choice of the initial operation for an eye with both primary glaucoma and cataract is a recurring problem which has had scant attention. Many ophthalmologists routinely remove the cataract first, with or without preliminary iridectomy, hoping to control the glaucoma at the same time. Further surgical treatment, usually cyclodialysis, is relied on should the tension again become elevated. Other ophthalmologists perform some operation for glaucoma first, believing that later cataract extraction offers the best chance for ultimate vision. A few ophthalmic surgeons prefer to perform an anterior sclerectomy or inclusion of an iris pillar at the time the cataract is extracted.

The literature contains no statistical evidence indicating which procedure gives the best final result in an eye with primary glaucoma and cataract. Elschnig¹ and van Lint² suggested that if the tension in such an eye never rises above 35 mm of mercury and can be reduced to 20 mm with miotics, cataract extraction should be the first operation, otherwise, cyclodialysis should be performed, followed in four weeks by extraction of the lens. Spaeth³ states that preliminary iridectomy and subsequent cataract extraction should be done only if the glaucoma is clearly secondary to swelling of the lens. If there is any question that the glaucoma is primary and noninflammatory, he believes that it is always best to perform an anterior fistulizing operation first and to remove the cataract later.

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and the Johns Hopkins University School of Medicine.

Read at the Forty-Ninth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology, Chicago, Oct 11, 1944.

¹ Elschnig, A. *Augenärztliche Operationslehre*, in Graefe, A., and Saemisch, T. *Handbuch der Augenheilkunde*, ed 3, Berlin, Julius Springer, 1922, vol 2, p 1240.

² van Lint, A., in Bailliart, P., and others. *Traité d'ophtalmologie*, Paris, Masson & Cie, 1939, vol 7 p 677.

³ Spaeth, E. B. *The Principles and Practice of Ophthalmic Surgery*, ed 3, Philadelphia Lea & Febiger, 1944, p 593.

O'Brien⁴ prefers to perform anterior sclerectomy at the time the cataract is extracted, and he has been pleased with his results. Kirby⁵ believes that the intraocular tension should be as nearly normal as possible before cataract extraction. If the tension is above normal, he performs a fistulizing operation at least six weeks before cataract extraction. If the tension is still above normal, a second operation for glaucoma is performed prior to extraction. If the tension is normal at the time of extraction, Kirby avoids the filtering area by making a corneal section in front of the bleb, but if the fistulizing operation has resulted in actual hypotension (8 mm of mercury or below), he makes his section through the filtering area, in the hope that as healing proceeds there may be some increase in tension.

The present study indicates the results obtained at the Wilmer Institute with various surgical procedures for different types of primary glaucoma with cataract.

MATERIAL

The case histories of all patients with the combination of primary glaucoma and cataract uncomplicated by other ocular disease who were operated on at the Wilmer-Ophthalmological Institute between Jan 1, 1927 and Jan 1, 1944 were reviewed. The lenticular changes varied from opacities of such degree that it was apparent later extraction would be indicated to hypermature cataracts. The histories were discarded if the follow-up period was less than six months after cataract extraction if that was the only operation, or less than six months after the second procedure if an operation for glaucoma was also performed. There was no other basis for the selection of cases. Forty-four case histories met the requirements for this study. The average follow-up period was nineteen months. The average age of the patients was 68 years.

ANALYSIS OF RESULTS

In the 44 cases studied there were (1) 29 eyes with chronic noncongestive glaucoma, (2) 10 with chronic congestive glaucoma and (3) 5 with

⁴ O'Brien, C. S. Personal communication to the author.

⁵ Kirby, D. B. *Prevention and Handling of Complications Arising During and After Cataract Extraction*, Arch Ophth 25:866-901 (May) 1941.

acute congestive glaucoma. The eyes with chronic noncongestive glaucoma were subdivided into two groups: (a) 21 in which the glaucoma could not be controlled with miotics and (b) 8 in which the glaucoma could be controlled with miotics.

The glaucoma was eventually controlled in 39 of these eyes, while in 5 it progressed to absolute glaucoma in spite of operation. The efficacy of the various procedures used depended in large measure on the type and stage of the glaucoma.

Chronic Noncongestive Glaucoma not Controllable with Miotics—The results of various

of miotics, and in a third miotics were necessary after both iridencleisis and trephination. In the last 2 eyes the tension rose after subsequent cataract extraction but was controlled in both instances with a single cyclodialysis and pilocarpine. In these 14 eyes an initial fistulizing operation followed by cataract extraction gave satisfactory results, later miotics or cyclodialysis being required in only 3 instances.

In 6 eyes the initial operation was a combined cataract extraction, 3 intracapsular and 3 extracapsular extractions. In all these eyes the tension became elevated within six weeks and

TABLE 1—*Results of Operative Procedures, Including Cataract Extraction, in Twenty-One Cases of Primary Chronic Noncongestive Glaucoma Not Controllable with Miotics*

Operative Procedure	Total Number of Cases	Postoperative Results			
		Tension Controlled Without Miotics	Tension Controlled With Miotics	Tension Controlled After Additional Operation for Glaucoma	Tension Not Controlled
Anterior fistulizing operation and later cataract extraction	14	11	1	2	
Combined cataract extraction	6			3	3
Combined cataract extraction with anterior sclerectomy (single procedure)	1	1			
Total number of cases	21	12	1	5	3

TABLE 2—*Results of Operative Procedures, Including Cataract Extraction, in Eight Cases of Primary Chronic Noncongestive Glaucoma Controlled with Miotics*

Operative Procedure	Total Number of Cases	Postoperative Results			
		Tension Controlled Without Miotics	Tension Controlled With Miotics	Tension Controlled After Additional Operation for Glaucoma	Tension Not Controlled
Combined cataract extraction	7	4	2	1	
Combined cataract extraction with inclusion of iris pillar	1				1
Total number of cases	8	4	2	1	1

operations in the 21 eyes with chronic noncongestive glaucoma not controllable with miotics are given in table 1. Fourteen of these eyes were subjected to an anterior fistulizing operation as the initial procedure, the cataract being extracted from three weeks to several years afterward. In 11 of these 14 eyes an initial trephination controlled the tension without miotics, and in all 11 the tension remained normal without miotics after subsequent cataract extraction. In 1 eye a Lagrange anterior sclerectomy controlled the tension without miotics, but after cataract extraction the tension again rose, although it could be controlled with pilocarpine. In another eye trephination controlled the tension only with use

of miotics. A trephination controlled the tension in 1 of them, and a single cyclodialysis and pilocarpine, in 2 others. One eye was almost blind from glaucoma before cataract extraction and was not operated on again. Two others did not respond to cyclodialysis but progressed to absolute glaucoma.

The initial procedure in 1 eye was a combined extracapsular cataract extraction and anterior sclerectomy. Tension afterward remained normal, without miotics.

Thus, in cases of primary noncongestive glaucoma with cataract, when the glaucoma was uncontrolled with miotics, an initial fistulizing operation prior to the extraction of the cataract

gave uniformly good results, while an initial cataract extraction in no instance controlled the tension and later operative procedures for the glaucoma were successful in only 3 instances.

Chronic Noncongestive Glaucoma Controlled with Miotics—The results of various operative procedures in the 8 eyes of this type are shown in table 2.

In 7 of these eyes a combined cataract extraction was the initial procedure, the extraction being intracapsular in 6 and extracapsular in 1. Tension remained normal after operation

In 6 of these eyes an anterior fistulizing operation was performed first, the cataract being extracted in from ten days to four years later. In 2 the fistulizing operation controlled the glaucoma, and the tension remained normal without miotics after cataract extraction. In the third a trephination controlled the tension but it became elevated after subsequent cataract extraction, and later cyclodialysis was required to control the glaucoma. In 3 eyes the tension was not controlled by the initial fistulizing operation and remained elevated after later cataract extrac-

TABLE 3.—Results of Operative Procedures, Including Cataract Extraction, in Ten Cases of Primary Congestive Glaucoma Not Controlled with Miotics

Operative Procedure	Total Number of Cases	Postoperative Results			
		Tension Controlled Without Miotics	Tension Controlled With Miotics	Tension Controlled After Additional Operation for Glaucoma	Tension Not Controlled
Anterior fistulizing operation and later cataract extraction	6	2		4	
Combined cataract extraction	4	3		—	1
Total number of cases	10	5	—	4	1

TABLE 4.—Results of Operative Procedures, Including Cataract Extraction, in Five Cases of Primary Acute Congestive Glaucoma Not Controlled with Miotics

Operative Procedure	Total Number of Cases	Postoperative Results			
		Tension Controlled Without Miotics	Tension Controlled With Miotics	Tension Controlled After Subsequent Operation for Glaucoma	Tension Not Controlled
Anterior fistulizing operation and later cataract extraction	1	1			
Combined cataract extraction	2	2			
Iridectomy with later cataract extraction	2	2			
Total number of cases	5	5	—	—	—

without miotics in 4 eyes and with pilocarpine in 2 others. In the seventh eye a later trephination controlled the tension.

In the last eye of this group a combined intracapsular extraction with inclusion of an iris pillar was the initial procedure. The tension again became elevated within two weeks, and the patient did not submit to further operation.

Chronic Congestive Glaucoma—The results of various operative procedures in 10 eyes with chronic congestive glaucoma and cataract are shown in table 3. The tension could not be controlled with miotics prior to operation in any of these eyes. In all there was a history or evidence of former attacks of low grade congestive glaucoma and the anterior chamber was shallow.

It was eventually controlled in all these cases by additional operations for glaucoma.

In 4 of these eyes a combined cataract extraction (intracapsular in 2 and extracapsular in 2 cases) was the initial operation. The tension was normal thereafter in 3 without miotics. In the remaining eye the tension rose within two weeks, and vision was already so impaired from the glaucoma that further operative intervention was not thought justifiable.

Acute Congestive Glaucoma—The results of the various operative procedures in 5 eyes with acute congestive glaucoma and cataract are shown in table 4.

In 2 eyes combined extracapsular cataract extractions were performed as the initial procedure because it was thought that the lens was

swollen and was a contributing cause of the glaucoma. In both instances the tension was normal thereafter without miotics. In 2 eyes iridectomy controlled the tension without miotics, and in the fifth eye iridencleisis achieved this result. Subsequent cataract extraction was not followed by an increase in tension in any of these eyes.

COMMENT

This series of cases is too small to permit definite conclusions, but it does indicate the general reaction of eyes with different types of glaucoma complicated by cataract to various operative approaches.

If the glaucoma is noncongestive and cannot be controlled with miotics, an anterior fistulizing operation with subsequent cataract extraction appears to give the best results. Thus, the glaucoma was controlled in all 14 eyes treated in this way, and in 11 of them miotics were not needed. Of 6 eyes in which cataract extraction was the initial operation, the tension was controlled in 3 only after subsequent operation for glaucoma and was never controlled in the other 3 eyes.

If the glaucoma is noncongestive and can be controlled with miotics, a combined cataract extraction will usually control the glaucoma, and the eye need be subjected to only one operation. Extraction, therefore, seems indicated as the initial procedure for this type of glaucoma.

In eyes with chronic congestive glaucoma a combined cataract extraction as the initial procedure offers at least as much chance of controlling the tension as, and probably more than, an anterior fistulizing operation performed first.

In eyes with acute congestive glaucoma it seems best to do an iridectomy followed by cataract extraction or a combined cataract extraction if the tension is not too high or if the lens appears to be greatly swollen.

I have hesitated to perform an anterior fistulizing operation at the time of cataract extraction because of the delay in reformation of the anterior chamber and the possibility of the development of extensive anterior synechias. Therefore, no evaluation of this surgical procedure is possible in this series.

An interesting incidental observation was that making an incision for cataract through an anterior fistulizing bleb had no apparent bad effect. In 16 of the eyes in this series an anterior fistulizing operation was performed and controlled the tension without miotics prior to cataract extraction. A Graefe section was made through the bleb in 9 of these eyes, and a subsequent operation for glaucoma was necessary in only 1 instance. The section was made in front of the bleb in 7 eyes, and a subsequent operation for glaucoma was necessary in 1 eye. A study of the eyes in which a section was made through the filtering area showed that such a procedure did not necessarily, or even usually, reduce filtration appreciably, but theoretically filtration should be reduced more by this procedure than by making the section in front of the bleb. It seems wise, therefore, to adhere to Kirby's⁵ tenet that the section should be made through the bleb if actual hypotension is present and in front of the bleb if tension is within normal limits.

SUMMARY

Results of operative procedure in 44 eyes with primary glaucoma and also cataract are analyzed. The following conclusions are drawn:

1. If the glaucoma is noncongestive and cannot be controlled with miotics, an anterior fistulizing operation should be performed prior to cataract extraction.

2. If the glaucoma is noncongestive but can be controlled with miotics, or if it is chronic congestive, a combined cataract extraction should be the initial procedure and is likely to be the only operation necessary.

Wilmer Ophthalmological Institute

RESECTION OF THE LEVATOR PALPEBRAE MUSCLE FOR PTOSIS WITH ANATOMIC STUDIES.

RAYNOLD N BERKE, MD
HACKENSACK, N J

From a review of the literature on surgical treatment for ptosis, one is forced to the conclusion that every operation devised for the cure of this condition has one or more disadvantages. This must necessarily be so because of the inherent nature of ptosis.

Ptosis may be defined as a drooping of the upper lid, from whatever cause. It may be acquired or congenital, unilateral or bilateral, partial or complete. Acquired ptosis is usually due to disease of the upper lid, to disease of the levator palpebrae muscle or to disease of the nervous system. Congenital ptosis is due to a developmental failure of the levator muscle or, according to some investigators, of the nucleus of the third nerve.

The 80 odd surgical procedures suggested for the cure of ptosis may be divided into three categories: first, utilization of the frontalis muscle to support the lid; second, employment of the superior rectus muscle to lift the lid; and third, shortening of the levator palpebrae muscle to enhance its lifting power. None of these surgical procedures gives entirely satisfactory results. The operations in which the frontalis muscle is utilized to support the lid produce an unnatural appearance of the lid. Those in which the result depends on formation of adhesions between the superior rectus muscle and the upper lid often produce hypertropia and lagophthalmos. Of the various surgical procedures proposed, those designed to enhance the lifting power of the levator muscle are to be preferred when this muscle is not completely paralyzed. The chief argument against resection of the levator palpebrae muscle arises from the fact that inadequate correction sometimes results. The purpose of this paper is to determine, if possible, the reasons for such failures.

OPERATIONS FOR RESECTION OF THE LEVATOR PALPEBRAE MUSCLE

All surgical procedures designed to increase the lifting power of the levator muscle consist

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in shortening this muscle, either by tucking its tendon or by excising a part of it. The operative approach may be through the conjunctiva or through the skin.

Resection of the Levator Muscle or Its Attachments Through the Conjunctiva—Bowman was perhaps the first to perform this operation. His technic was recorded by Mr Bader, the curator and registrar of the Royal London Ophthalmological Hospital in a report for the year ending Sept 25, 1857.¹ Six operations for ptosis had been done that year, 4 of which consisted in the "usual operation of removal of an oval piece of skin" from the upper lid. The report stated:

In one case in which this operation had been done with an unsatisfactory result, Mr Bowman applied a new plan—he everted the lid and excised the posterior or upper edge of the palpebral cartilage, with about half an inch (1 cm) of the tendon of the levator palpebrae inserted into it. Before actual removal of the piece, very fine threads were passed so as to bring together the edges, and then secure a shortening of the tendon of the levator muscle, to the extent of three-quarters of an inch (19 cm). It is to be expected that it will be permanently shortened, and be enabled to assist in raising the lid. The upper cul de sac of the conjunctiva is exposed to little movement, and wounds there readily heal. The lid was turned back to its natural position.

This is the first record of an attempt to correct ptosis by resection of the levator muscle. From the description of this operation it is certain that Muller's muscle was resected. Whether the tendon of the levator palpebrae muscle was also included in the resection is difficult to say, because of Bowman's failure to differentiate Muller's muscle and the tendon of the levator muscle. A careful search of Bowman's publications showed that he made no distinction between this tendon (aponeurosis) and Muller's muscle.

Wheeler² performed, but did not publish, a somewhat similar procedure for resection of

¹ Bowman, W. Rep Roy London Ophth Hosp 1 34-35, 1859

² Wheeler, J. M., cited by Meek, R. E. Applied Anatomy of the Eye. Its Relation to Ophthalmic Surgery, Arch Ophth 26 494-513 (Sept) 1941

the levator muscle His technic is essentially that described by Bowman, as follows The lid is everted with an Ehrhardt clamp, an incision is made through the conjunctiva 1 mm above the upper margin of the tarsus, and the conjunctiva is freed from Muller's muscle approximately 10 to 15 mm upward An incision is then made through the tarsus 2 or 3 mm from the upper margin Muller's muscle, which is attached to this narrow strip of tarsus, and presumably also the tendon of the levator muscle lying anterior, are then dissected backward by following the normal line of cleavage between the levator muscle and the posterior surface of the orbicularis muscle Three double-armed silk sutures are then passed through the conjunctiva near its cut edge and through the levator muscle 10 to 12 mm above the tarsus The muscle is then excised anterior to the sutures, and the three double-armed sutures are passed through the upper border of the cut edge of the tarsus and then through the skin and finally tied over rubber pegs A petrolatum dressing is applied, and the sutures are removed on the fourth or fifth day In 1917 Maddox³ modified the Bowman operation by exposing Muller's muscle through the conjunctiva, cauterizing it and then tucking it with three sutures, so that it would be permanently shortened

In 1896 Wolff⁴ described an operation for resection of Muller's muscle⁵ He double everted the lid, made a horizontal incision through the upper portion of the conjunctival cul-de-sac and exposed Muller's muscle by reflecting the conjunctiva downward Vertical incisions, 10 to 12 mm apart, were made through the muscle, which was lifted up on strabismus hooks Two surgical gut sutures were passed through the muscle and tied The muscle was cut below the sutures, which were passed through the upper border of the tarsus, tied and cut short The amount of resection required was equal to the difference in width between the two palpebral fissures The conjunctiva was closed by means of five surgical gut sutures

³ Maddox, E. E. A New Operation for Ptosis, Brit J Ophth 1:358-362, 1917

⁴ Wolff, H. Die Vorlagerung des Musc levator palp sup (Musc Mulleri) mit Durchtrennung der Insertion, Arch f Augenh 33:125-144, 1896

⁵ Wolff recognized the difference between the tendon of the levator muscle and Müller's muscle and described two procedures for the correction of ptosis first, resection of Müller's muscle through the conjunctiva, and, second, resection of the tendon of the levator muscle through the skin.

In 1909 Blaskovics first described his operation for resection of the levator muscle through the conjunctiva His latest procedure⁶ consists in everting the lid, injecting 2 cc of a 2 per cent solution of procaine hydrochloride containing epinephrine hydrochloride under the upper fornix of the conjunctiva and incising the latter 2 or 3 mm above the upper border of the tarsus Three double-armed sutures are placed through the cut edge of the conjunctiva, and the latter is dissected free from Muller's muscle with scissors, using the three sutures for traction Three other sutures are placed through Muller's muscle and presumably also through the tendon of the levator muscle 2 to 3 mm above the tarsal border, and the muscle is cut free from the tarsus By traction on these fixation sutures the attachments of the levator muscle are freed from the conjunctiva, on one side, and the "pretarsal tissues," on the other, so that the levator muscle can be pulled out easily The three double-armed sutures in the conjunctiva are then passed through the levator muscle "at the correct height," and the muscle is excised distal to the sutures The lid is now turned back with the cutaneous surface anterior, the lid is retracted upward to expose the levator muscle, and three mattress sutures are placed through the anterior surface of the muscle 4 to 5 mm above the cut edge With scissors the upper half of the tarsus is excised (all but 1 5 mm of the tarsus may be removed if necessary), and the sutures are passed through the skin, the sutures in the upper part of the muscle are passed through the skin 5 to 6 mm above the margin of the lid, and the sutures in the lower edge, through the skin at the upper cut edge of the tarsus If the lower sutures are placed too near the lashes, ectropion will result, if too high, the skin will fall over the lashes and scratch the cornea The two sets of sutures are tied, and the lower set is cut off The upper set is used as traction sutures, to pull the upper lid down over the cornea for protection, and anchored with adhesive plaster to the cheek An ordinary petrolatum dressing is applied, which is replaced with a Fuchs shield in twenty-four hours All sutures are removed on the sixth day

All four procedures just described were resections of Muller's muscle Each surgeon thought that he was excising a part of the

⁶ von Blaskovics, L. A New Operation for Ptosis with Shortening of the Levator and Tarsus, Arch Ophth 52:563-573, 1923, Treatment of Ptosis Formation of a Fold in the Eyelid and Resection of the Levator and Tarsus, ibid 1:672-680, 1929, Eingriffe am Auge, Ferdinand Enke, Stuttgart, 1938, pp 174-179

levator muscle Only Wolff differentiated Müller's muscle from the aponeurosis and from the levator muscle It is possible that the other operators may have been familiar with the difference between the levator muscle and Müller's muscle, but their failure to differentiate these structures, their descriptions and their illustrations make this doubtful

In 1942 Agatston⁷ modified the Blaskovics procedure, stating that he resected Müller's muscle and the aponeurosis of the levator muscle together In his procedure the lid is everted and an incision made through the tarsus 3 mm from its upper margin The upper part of the tarsus is then dissected upward with scissors, Müller's muscle being cut from the tarsus The conjunctiva, still attached to the tarsus, is dissected back to the upper fornix Müller's muscle and the aponeurosis are picked up with forceps, and the tendon is dissected free from the orbicularis muscle up to the areolar tissue of the orbit Three double-armed sutures are passed from the conjunctival surface through Müller's muscle and the aponeurosis several millimeters above the cut edge, and the two attachments of the levator muscle are cut off 2 to 5 mm anterior to the sutures The sutures are then passed anterior to the tarsus and out through the skin, where they are tied over a roll of gauze 2 mm from the lashes The part of the tarsus still attached to the conjunctiva is now cut off, and the conjunctiva is approximated to the upper margin of the tarsus with a running silk suture This is the only operation for ptosis in the literature in which the author claimed to resect both the aponeurosis of the levator muscle and Müller's muscle Other surgeons may have included both insertions of the levator muscle in their resections, referring to them as the "levator muscle," but their failure to differentiate these structures from the levator muscle itself leads to confusion

Tucking or Folding of the Aponeurosis of the Levator Muscle—In 1883 Eversbusch⁸ described an operation in which the action of the levator muscle was enhanced by folding the tendon on itself With the patient under general anesthesia, a Snellen clamp was applied and an incision made through the skin, the orbicularis muscle and the septum orbitale, halfway between the border of the lid and the

⁷ Agatston, S A Resection of the Levator Palpebrae Muscle by Conjunctival Route for Ptosis Simplified Technic, Arch Ophth **27** 994-996 (May) 1942

⁸ Eversbusch, O Zur Operation der congenitalen Blepharoptosis, Klin Monatsbl f Augenh **21** 100-107, 1883

brow The upper and the lower lip of the incision were separated to expose the tendon of the levator muscle and the anterior surface of the tarsus A double-armed suture was passed through the central part of the tendon 3 to 4 mm from the upper border of the tarsus Two similar sutures were inserted on each side of the central suture 3 mm from it All three double-armed sutures were then passed between the tarsus and the skin and out through the gray line of the lid Before they were tied the clamp was removed and the cutaneous incision closed with three other sutures Tightening the sutures caused the tendon to fold on itself anterior to the tarsus When a redundancy of skin existed, a strip of skin and of orbicularis muscle was excised, to lessen the weight of the lid and the antagonistic action of the orbicularis muscle

Snellen⁹ suggested two operations for tucking the levator muscle, the first of which was like the Eversbusch procedure and the other did not employ a cutaneous incision In the latter procedure he passed three sutures from the surface of the skin through the lid just above the tarsus The needles were then carried up to the fornix, directed downward between the skin and the tendon of the levator muscle and out through the skin 2 mm from the point of entrance, they were finally tied over beads or pieces of tubing Wilder¹⁰ and Beard¹¹ each described an operation for tucking the tendon of the levator muscle and the septum orbitale by means of two sutures placed between the tarsus and the frontalis muscle, they thus combined shortening of the levator muscle with utilization of the frontalis muscle Except for Eversbusch's operation, none of these tucking procedures attained wide acceptance, and today practically all have been replaced by other methods

Shortening of the Levator Muscle by Excising a Part of the Lid—Any operation in which a part of the tarsus is excised results in actual shortening of the levator muscle and should be included here The ancient Arabian procedure of excising a piece of skin from the upper lid was seldom successful¹² because the skin

⁹ Snellen, H New Method of Treating (1) Symblepharon, (2) Ptosis, and (3) Episcleritis, Tr Ophth Soc U Kingdom **10** 207-210, 1890

¹⁰ Wilder, W H Operation for Ptosis, Tr Am Ophth Soc **8** 99-102, 1897

¹¹ Beard, C H Ophthalmic Surgery, ed 2, Philadelphia, P Blakiston's Son & Co, 1914, pp 230-252

¹² Wilder, W H Operations for the Relief of Trichosis, Entropion, Ptosis and Epicanthus, in Wood, C A A System of Ophthalmic Operations, Chicago, Cleveland Press, 1911, vol 2, pp 1523-1563

stretched so as to neutralize the effect of the operation. If enough skin was removed to effect permanent widening of the palpebral fissure, lagophthalmos, corneal ulceration and sometimes loss of the eye resulted. In 1863 von Graefe¹³ modified the ancient Arabian procedure slightly by removing an elliptic piece of orbicularis muscle instead of skin from the upper lid. Two years later Bowman,¹⁴ apparently not satisfied with his first attempt to correct ptosis by resection of the levator muscle through the conjunctiva, proposed resection through the skin. He made an incision through the skin, which he reflected upward and downward, then excised an oval piece of orbicularis muscle, tarsus and conjunctiva and sewed the edges together. Gillet de Grandmont¹⁵ accomplished the same thing by placing the cutaneous incision 2 or 3 mm above the margin of the lid instead of 8 mm above, as was done by Bowman. Nicati,¹⁶ Boucheron,¹⁷ Gruening,¹⁸ Theobald¹⁹ and Mayou²⁰ resected a piece of the tarsus. Fergus²¹ removed skin, orbicularis muscle and tarsus but spared the conjunctiva. Galezowski²² removed skin, orbicularis muscle, tarsus and conjunctiva.

Resection of the Tendon of the Levator Muscle Through the Skin.—In 1896 Wolff⁴ described a simple method for shortening the tendon of the levator muscle. A cutaneous incision, 2 cm long, was made at the level of the upper border of the tarsus, and the skin was dissected free from the orbicularis muscle 3 to 4 mm upward and downward. The orbicularis

13 von Graefe, A. Operation der Ptosis, Arch f Ophth **9** (pt 2) 57-78, 1863

14 Bowman, W. Rep Roy London Ophth Hosp **2** 111-112, 1861

15 Gillet de Grandmont. Nouvelle operation du ptosis congenital, Bull et mem Soc fran^c d'opht **9** 80-83, 1891

16 Nicati, W. Operation de ptosis par avancement de l'insertion du releveur palpebrale, Arch d'opht **10** 162-163, 1890

17 Boucheron, M. Operation du ptosis, Arch d'opht **8** 229, 1888, cited by von Blaskovics⁶

18 Gruening, E. C. The Value of Partial Resection of the Tarsal Cartilage in the Operative Treatment of Congenital Ptosis, Tr Am Ophth Soc **9** 574-576, 1902; Treatment of Various Forms of Ptosis by Partial Resection of the Tarsal Cartilage, New York Eye & Ear Infirmary Rep **11** 1-3, 1904

19 Theobald, S. A Simplification of Grandmont's Operation for Ptosis, Tr Am Ophth Soc **11** 673-677, 1908

20 Mayou, M. S., in Burghard, F. F. A System of Operative Surgery, ed 1, London, H. Frowde, 1909, vol 4, pp 267-274

21 Fergus, A. T. Ptosis Operations Tr Ophth Soc U Kingdom **28** 184-190, 1908

muscle and the underlying septum orbitale were grasped with forceps and freed from the upper border of the tarsus and the aponeurosis of the levator muscle. Two vertical incisions were made about 10 mm apart through the aponeurosis of the levator muscle, and two squint hooks were passed beneath the tendon of the muscle. The tendon was then freed from the underlying Muller's muscle, two double-armed surgical sutures were passed through the tendon several millimeters above its attachment to the tarsus and the sutures tied. The tendon anterior to the sutures was excised, the cut edge sutured to the upper border of the tarsus and the skin closed with three or four silk sutures. Wolff recommended 1 mm of resection for each millimeter of ptosis. De Lapersonne²³ modified the Wolff resection by combining advancement of the insertion with resection of the levator muscle. Instead of attaching the cut edge of the tendon of the levator muscle to the upper margin of the tarsus, he carried the tendon down 2 or 3 mm from the margin of the lid by passing the sutures through the anterior surface of the tarsus at this point. A piece of skin and orbicularis muscle was sometimes removed before closing the skin. Elschnig²⁴ resected the tendon of the levator muscle in almost the same way as was outlined by de Lapersonne except that he placed the cutaneous incision 10 mm above the convex border of the tarsus, rather than 3 to 4 mm below it. In 1919 Lancaster²⁵ designed an operation for shortening the levator muscle through the cutaneous route, in which a piece of skin to which the levator muscle was attached was excised, along with the tendon of the levator muscle.

The operations just described are a fairly complete list of the various surgical procedures proposed for increasing the lifting power of the levator muscle. Only a few of these operations are used today, the most popular of which seems to be the Blaskovics and the Wheeler procedure. The Blaskovics technic is the method generally employed for resection of the levator muscle at Stanford University Hospitals,²⁶ and Greens' Eye Hospital, San Fran-

23 de Lapersonne, F. Sur quelques modifications dans les operations du ptosis, Arch d'opht **23** 497-502, 1903

24 Elschnig, A. Ptosisoperationen, in Elschnig, A., and Axenfeld, T. Handbuch der gesamten Augenheilkunde, Berlin, Julius Springer, 1922, vol 1, pp 243-280

25 Lancaster, W. The Operative Treatment of Ptosis, Am J Ophth **3** 457, 1920

26 Bettman, J. W. Personal communication to the author

cisco²⁷, Passavant Memorial Hospital, Chicago²⁸, Illinois Eye and Ear Infirmary, Chicago²⁹, University Hospital, Ann Arbor, Mich³⁰, University Hospitals, Minneapolis,³¹ and Wills Hospital, Philadelphia³². At the Presbyterian Hospital, New York, the Wheeler procedure is the method of choice³³. At none of these hospitals is Muller's muscle differentiated from the tendon of the levator muscle during the operation.

INDICATIONS FOR RESECTION OF THE LEVATOR MUSCLE

Not all cases of ptosis are suitable for resection of the levator muscle. Most authors³⁴ agree that some action of this muscle is necessary to insure success of the operation. Blaskovics⁶ maintained that his procedure could be used for all types and degrees of ptosis with complete satisfaction, "even when the muscle is absent," and that "an apparent function of the levator develops even in those cases in which this muscle was completely paralyzed or atrophic." It is difficult for me to conceive how an absent muscle can be resected or made to function effectively.

There are two methods of determining the functional state of the levator muscle. First, one can study the action of the upper lid. If the lid is elevated, the palpebral fissure widened or the fold of the upper lid deepened in upward gaze, while the frontalis muscle is kept from acting, there is presumptive evidence that the

27 Green, M I Personal communication to the author

28 Gifford, S R Personal communication to the author

29 Gradle, H Personal communication to the author

30 Fralick, F B Personal communication to the author

31 Burch, F E Personal communication to the author

32 Spaeth, E B Personal communication to the author

33 This survey is incomplete and is intended to indicate only a trend. I obtained this information from personal communications.

34 (a) Wheeler, J M Personal communication to the author (b) Dunnington, J H Blepharoptosis Its Surgical Treatment, M Rec & Ann 35 880-883, 1941 (c) Kirby, D B Blepharoptosis The Technique of Its Surgical Correction, Surg, Gynec & Obst 70 438-449, 1940 (d) Spaeth, E B Principles of Ophthalmic Surgery, ed 1, Philadelphia Lea & Febiger, 1939 (e) Wiener, M, and Alvis, B Y Surgery of the Eye, Philadelphia, W B Saunders Company, 1939 (f) Koster, W Zur Untersuchung der Muskelverhältnisse des oberen Lides bei Ptosis congenita, Ztschr f Augenh 3 304, 1900, Die verhinderung van den musculus tarsalis sup bij ptosis congenita, Nederl tijdschr v geneesk 2 417, 1900 Wilder¹²

levator muscle is present and active. Second, according to Koster,³⁴ widening of the fissure after the instillation of a few drops of cocaine indicates that Muller's muscle and the levator muscle are present.

ESTIMATION OF THE AMOUNT OF RESECTION FOR 1 MM OF PTOSIS

Wolff⁴ stated that 1 mm of resection of the levator muscle would correct 1 mm of ptosis. Kirby³⁴ estimated that 1 mm of ptosis could be corrected by 2 mm of resection of the levator muscle or by 1 mm of resection of the tarsus, but added that "it is best to do a little more than this." Green³³ followed the same rule in estimating the amount of shortening necessary. Blaskovics⁶ stated that less than 5 mm of resection has no effect and that no rule can be made for all cases because the effect of all operations for shortening becomes greater with each additional millimeter of resection. In estimating the amount of shortening to be done one must consider the elasticity of the levator muscle, the weight of the lid, the length of the fissure, the rigidity of the skin, the presence of epicanthus or endophthalmitis and the age of the patient. By pulling on the freed tendon to test its strength and elasticity, Blaskovics estimated the amount of resection necessary. When the levator muscle is elastic as much as 20 mm may have to be removed for a satisfactory result. When the levator muscle is replaced by scar tissue, more than 10 mm cannot be removed. If a greater amount must be resected additional tarsal tissue must be removed. The amount of tissue excised must be measured when the muscle is relaxed, and not when it is stretched by traction.

ADVANTAGES AND DISADVANTAGES OF OPERATIONS ON THE LEVATOR MUSCLE

According to Dunnington,^{31b} Malbran³⁶ and others, shortening of the attachments of the levator muscle in selected cases is the best procedure to use in the repair of ptosis, for the following reasons: (1) Postoperative reaction is negligible, (2) lagophthalmos is almost absent, (3) the lid moves with the globe normally in all directions of gaze, (4) the margin of the lid is not deformed, (5) a good lid fold is produced, (6) the procedure can be used in repair of congenital ptosis even when accompanied with epicanthus, (7) no backward tilt of the head or elevation of the brow results, (8) there is no diplopia after operation due to weakening

35 Green, M I Modified Blaskovics Operation for Ptosis, Bull Pract Ophth 12 7-9, 1942

36 Malbran, J La corrección operatoria de la ptosis palpebral, Semana med 2 1456-1462, 1941

of the superior rectus muscle, (9) the method can be used when the superior rectus muscle is weak, (10) and the winking reflex is not disturbed.

The disadvantages of shortening the levator muscle are as follows: 1. The operation can be used successfully only when the levator muscle is present and active. 2. There is a tendency to undercorrection. 3. Lagophthalmos may result if too much tissue is removed.

RESULTS OF SHORTENING THE LEVATOR MUSCLE

In 1923 Blaskovics⁶ reported on 21 operations which he had done by his method, with undercorrection in 1 case and overcorrection in 2 cases. In 5 cases there had been total paralysis, in 4 cases, paresis, in 2 cases, an inflammatory condition, in 2 cases, ptosis as a result of trauma, in 4 cases, congenital ptosis and in 4 cases, congenital ptosis with epicanthus. In 1929 he added 12 more cases, in all of which "excellent results" were obtained. Lindner³⁷ used the Blaskovics operation in 19 cases, the results being excellent in 12 cases, good in 5 cases and unsatisfactory in 1 case, the condition being made worse in 1 case. In 3 cases the operation had to be repeated. Jaensch³⁸ did this operation in 19 cases, with improvement in all but 1 case. For comparison, the author reviewed the results in 42 cases of ptosis in which resection of the levator muscle was done according to the Wheeler technic. In 30 cases improvement resulted, in 10 cases there was no improvement, and in 2 cases the ptosis was worse. This high percentage of failures was disturbing and led to an examination of the possible causes for such failure.

REASONS FOR FAILURE OF RESECTION OR THE LEVATOR MUSCLE

Among the reasons that resection does not always give a satisfactory correction are the following possibilities: 1. The levator muscle may be too weak to support the lid. In some cases this may be true, especially if no action of this muscle is present. It is obviously impossible to determine before operation the histologic or anatomic condition of the levator muscle. Knowledge of the state of this muscle is therefore entirely dependent on the physiologic behavior of the upper lid. Tests to measure its activity give no information as to the size of the levator muscle, its elasticity, its tensile

strength or the presence of fibrosis, degeneration or congenital anomalies of structure or innervation. These factors govern the success of the operation but cannot be determined before operation by physiologic or clinical tests. In acquired ptosis the muscle must be present, even though paralyzed. In cases of congenital ptosis, however, the levator muscle was described as absent or defectively developed by Heuck,³⁹ Bach,⁴⁰ Ahlstrom⁴¹ and Siemerling.⁴² Certainly, if this muscle is absent, an attempt to correct the ptosis by resection of the levator will lead to failure.

2. The sutures may pull out after operation and thus lead to failure. This accident is especially likely to occur if mattress sutures are not employed or if severe edema develops after operation. The danger of the sutures pulling out can be reduced to a minimum by using a double set, as advocated by Blaskovics, and by leaving a generous amount of the tendon anterior to the sutures. Postoperative edema can be minimized by avoiding unnecessary trauma during the operation.

3. An insufficient amount of the levator muscle may be resected in some cases, especially if the muscle is extremely elastic, the lid thick and heavy or the surgeon timid. Blaskovics called attention to the fact that the amount of resection needed must be determined at the time of operation by the condition of the levator muscle and the lid, rather than by a rule calling for so many millimeters of resection for so many millimeters of ptosis.

4. Resection of Muller's muscle instead of the tendon of the levator muscle may be responsible in some cases. Unfortunately, most textbooks on ophthalmic surgery do not differentiate these two structures or call attention to the possibility of this mistake being made during the operation. Even the sponsors of some operations for resection of the levator muscle have failed in this respect.

A brief study of the anatomic position of Muller's muscle will convince any one that every resection of the levator muscle done through

³⁹ Heuck, A. Ueber angeborenen vererbten Beweglichkeits-Defekt der Augen Fall IV, Klin Monatsbl f Augenh **17** 253-278, 1879.

⁴⁰ Bach, L. Anatomischer Befund eines doppelseitigen angeborenen Kryptophthalmos beim Kaninchen nebst Bemerkungen über das Okulomotoriuskerngebeit, Arch f Augenh **32** 16-32, 1892.

⁴¹ Ahlstrom, G. Doppelseitige kongenitale Ptosis und Unbeweglichkeit der Bulbi, Beitr z Augenh **2** 523-554, 1895.

⁴² Siemerling, E. Anatomischer Befund bei einseitiger congenitaler Ptosis, Arch f Psychiat **23** 764-774, 1892.

³⁷ Lindner, K. Ueber die Ptosisoperation nach Blaskovics, Klin Monatsbl f Augenh **93** 1-12, 1934.

³⁸ Jaensch, P. A. Zur Ptosisoperation, Klin Monatsbl f Augenh **94** 183-189, 1935.

the conjunctiva is, at least in part, a resection of Muller's muscle, for Muller's muscle lies between the conjunctiva and the tendon of the levator muscle. Few surgeons have recognized or called attention to this fact. Bowman, who performed the first resection of the levator muscle on record, "everted the lid and excised the posterior or upper edge of the palpebral cartilage, with about half an inch of the tendon of the levator palpebrae inserted into it." According to this description, he resected Muller's muscle. He may have included with Muller's muscle a piece of the aponeurosis, but his failure to differentiate these structures makes it doubtful. Blaskovics,⁶ after everting the lid and reflecting the conjunctiva, grasped the exposed "levator muscle" and freed it from the tarsus below, from the conjunctiva behind and from the "pretarsal" tissues in front. The muscle, which he called the "levator muscle," must have been Muller's muscle. It is conceivable that he may have pulled the levator muscle into the wound by strong downward traction and thus have resected a part of it. Or he may have placed his sutures deep enough in Muller's muscle to have included the aponeurosis and thus have resected it also. His failure to differentiate these structures is unfortunate. Maddox⁸ expressed vividly his conception of the levator muscle by saying:

After double eversion of the eyelid, nothing intervenes between the surgeon and the levator tendon but a thin loose layer of that peculiarly accommodating membrane, the conjunctiva, which is no sooner divided along the upper margin of the tarsus and reflected from the tendon, than the latter lies in full view, and can be shortened without interfering at all with the natural beauty of the front of the eyelid.

Obviously he was describing Muller's muscle.

The tissues of the upper lid above the tarsus from the inner surface out are (1) the conjunctiva, (2) Muller's muscle, (3) the aponeurosis of the levator muscle, (4) the septum orbitale, (5) the orbicularis muscle and (6) the skin (fig 1). It is therefore evident that the first structure encountered by the surgeon after the conjunctiva has been reflected is Muller's muscle, and not the levator muscle, as is so often stated by authors of operations for resection of the levator muscle. The levator muscle ends 10 or 12 mm from the tarsus and cannot be reached through the conjunctiva unless Muller's muscle and the aponeurosis are strongly pulled downward. What Bowman, Wolff, Blaskovics, Maddox and others described and illustrated as the levator was Muller's muscle. The question therefore arises: Did these surgeons resect only

Muller's muscle, or did they, unknowingly, resect also the aponeurosis of the levator muscle, which lies anterior to and loosely connected with Muller's muscle?

Because Muller's muscle has been so often confused with the levator muscle and with its tendon (aponeurosis), it is entirely possible that only Muller's muscle may have been resected in some cases. Considering the frail and delicate character of this muscle, it is probable, as suggested by Hildreth,⁴³ that this fact alone may have been responsible for some failures following supposed resection of the levator muscle.

The problem was approached in the following manner. First, the normal anatomy of the upper lid and the levator muscle was studied by dissection of orbits of cadavers in the usual three-dimensional manner—from the anterior, the lateral and the superior aspect. This investiga-

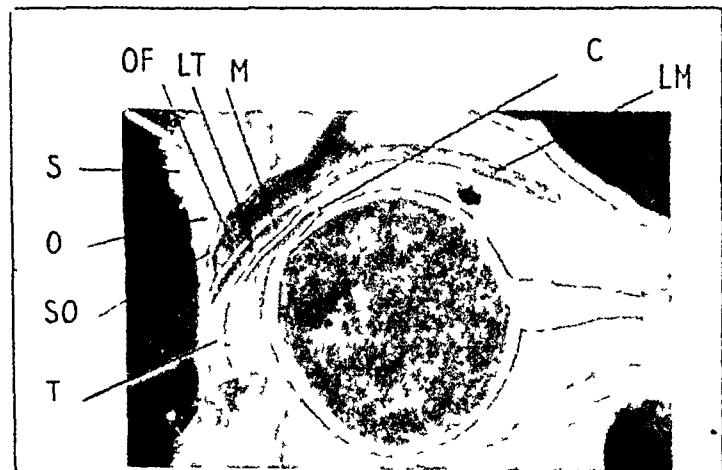


Fig 1.—Sagittal section through the orbit, showing the normal anatomic structure of the upper lid. The tissues have been separated to show the normal relation of the conjunctiva (C), Muller's muscle (M), the tendon of the levator muscle (LT), the septum orbitale (SO), the orbicularis muscle (O) and the skin (S). The section also shows the position of the tarsus (T), the orbital fat, removed (OF), and the levator muscle (LM) (retouched photograph of a specimen from a cadaver).

tion was supplemented by studies of gross sections of other cadaver orbits in the frontal, the sagittal and the horizontal plane. Second, an attempt was made to demonstrate the normal planes of cleavage between (a) the conjunctiva and Muller's muscle, (b) Muller's muscle and the tendon of the levator muscle and (c) the tendon and the septum orbitale. Different-colored material was placed between these three layers, the tissues were replaced in their normal positions, and the orbit was sectioned in the sagittal plane for study. Third, three types of operations for resection of the levator muscle

⁴³ Hildreth, H R. The Insertions of the Levator Palpebrae Muscle, Am J Ophth 24:749-758, 1941.

were done on cadavers in the routine manner, and the orbits were sectioned in the sagittal plane and then studied to determine what tissue or tissues had been removed

ANATOMY OF THE LEVATOR MUSCLE AND THE UPPER LID

With the textbooks of Whitnall,⁴⁴ Wolff⁴⁵ and others⁴⁶ as a guide, a detailed study of the normal anatomy of the upper lid and the levator muscle showed that the skin, the orbicularis muscle and the septum orbitale hang loosely from the superior orbital margin to the tarsus. The levator muscle arises at the apex of the orbit and runs forward in close contact with the underlying superior rectus muscle to above the globe, where the two become separated by a thickening of Tenon's capsule. At this point the aponeurosis and Muller's muscle begin and extend forward and downward for 10 to 12 mm., to the level of the upper border of the tarsus (fig 1).

More detailed study of these parts with a magnifying glass brings out the following facts:

1 The skin is firmly adherent to the underlying tissues at the brow and extends down to the margin of the lid, where it is again firmly adherent. Five to 10 mm. above the lashes it is thrown into a horizontal fold, the upper lid fold, by the terminal fibers of the aponeurosis of the levator muscle, which end here and serve to keep the loose skin of the upper lid from prolapsing over the lashes (fig 1). Elsewhere the skin is loosely attached to the underlying orbicularis muscle except at the internal and external canthal ligaments, to which it is firmly attached.

2 The orbicularis muscle is fused with the corrugator supercilii muscle and the frontalis muscle at the brow (fig 1). From here it extends downward to the margin of the lid, being loosely attached to the skin in front and to the septum orbitale behind. Anterior to the tarsus the orbicularis muscle is loosely adherent to the skin in front and to the tarsus behind, medially it is attached to the nasal margin of

the orbit and the internal canthal ligament and laterally to the bone of the temporal margin of the orbit by way of the external raphe. At the level of the upper lid fold it is fused with some of the terminal fibers of the aponeurosis of the levator muscle as they pass through the orbicularis muscle to become attached to the skin.

3 The septum orbitale begins at the orbital margin from the junction of the periosteum of the frontal bone and the periorbita of the orbit (fig 1). At this point it is thickest, and from here downward it becomes thinner, as it hugs the posterior surface of the orbicularis muscle. As a matter of fact, it seems more accurate surgically to conceive of this structure as the posterior fascial sheath of the orbicularis muscle rather than as a separate structure. At about the level of the upper border of the tarsus, the septum orbitale seems to end by fusing with the anterior surface of the aponeurosis of the levator muscle, thus forming a barrier to the prolapse of the orbital fat. Below the upper border of the tarsus and between the anterior surface of the tarsus and the posterior surface of the orbicularis, there is a thin layer of loose connective tissue, which occupies the same relation to the orbicularis muscle as does the septum orbitale above and which for practical purposes can be considered a prolongation of this membrane. Medially the septum orbitale is adherent to the nasal margin of the orbit and laterally to the temporal margin.

4 Posterior to the septum orbitale above the tarsus is the orbital fat (fig 1), which is comma-like in sagittal section, being thick and rounded in front and thin and pointed behind. It fills the interval between the sheath of the levator muscle, below, the roof of the orbit, above, and the septum orbitale, in front.

5 Below and behind this roll of orbital fat is the aponeurosis of the levator muscle, with a thin, transparent sheath of areolar tissue (fig 1), which blends with the septum orbitale. The aponeurosis arises from the anterior extremity of the terminal fibers of the levator muscle and extends forward and downward to the tissues of the upper lid anterior to the tarsus (fig 1). It is divided into a medial horn and a lateral horn. The former is thin and fragile and is difficult to follow in its course from the levator muscle to the upper border of the medial canthal ligament. In this position it is posterior to the septum orbitale and anterior to Muller's muscle. The lateral horn is more dense and fibrous; it extends from the lateral half of the

⁴⁴ Whitnall, S. E. Anatomy of the Human Orbit and Accessory Organs of Vision, ed 2, London, Oxford University Press, 1932, pp 115-192.

⁴⁵ Wolff, E. Anatomy of the Eye and Orbit, ed 2, Philadelphia, The Blakiston Company, 1940, pp 120-139.

⁴⁶ Eisler, P. Die Anatomie des menschlichen Auges in Schieck, F., and Brückner, A. Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol 1, pp 211-386. Wolff, H. Ueber die Sehne des Musculus levator palpebral superioris, Ztschr f Augenh 13 440 1905, 15 576, 1906.

levator muscle to the upper border of the external canthal ligament, posterior to the septum orbitale and anterior to Muller's muscle. It separates the lacrimal gland into two parts as it proceeds along its course, so that the main part of the gland lies above the lateral horn and the accessory lobe is behind it.

The middle part of the tendon of the levator muscle is the portion most concerned with operations for ptosis. It is about 10 to 12 mm long and extends from the anterior extremity of the levator muscle forward, between the orbital fat, above, and Muller's muscle, below, to the upper border of the tarsus. Here it divides into thousands of fine fibrillae, which become attached in small part to the anterior surface of the tarsus but chiefly to the overlying orbicularis muscle and the skin, thus producing the upper lid fold. The septum orbitale fuses with the anterior surface of the tendon of the levator muscle a short distance above the tarsus (fig 1).

Muller's muscle is about 10 or 12 mm long and extends from the levator muscle to the upper border of the tarsus (fig 1). At its origin from the levator muscle, 2 to 3 mm posterior to the origin of the aponeurosis, there is a gradual transition from striated to smooth muscle fibers. The muscle is about 0.5 mm thick and is delicate and easily torn. It is loosely adherent above to the aponeurosis and is adherent below to the conjunctiva.

The conjunctiva is firmly adherent to the tarsus below and is loosely attached to Muller's muscle above (fig 1). At the upper fornix it is supported by a thin sheath of connective tissue, extending forward from the conjoined sheaths of the levator and the superior rectus muscle, i.e., by the so-called suspensory ligament of the upper fornix.

With careful gross dissection of the upper lid, in sagittal sections especially, one observes three layers of tissue below the upper border of the tarsus, namely, the skin, the orbicularis muscle and the tarsus, with the adherent conjunctiva (fig 1). These layers can be easily separated surgically. Above the upper border of the tarsus, the orbital fat divides the tissues of the upper lid into two layers, so that anterior to the fat are the skin, the orbicularis muscle and the septum orbitale. Posteriorly there are the aponeurosis of the levator muscle, Muller's muscle and the conjunctiva. These layers can be easily identified and separated in the cadaver (fig 1).

For further study and identification of these planes of dissection, the following procedure was used to simulate as much as possible the conditions encountered surgically. The upper lid was everted and the conjunctiva dissected free from Muller's muscle for 10 to 15 mm. Then the upper border of the tarsus was incised, and the attachments of the levator muscle were dissected upward along the pretarsal fascial plane for a distance of 10 to 15 mm.⁴⁷ Two vertical incisions, about 15 to 20 mm apart, were then made through the pretarsal fascial tissues, and a tunnel was formed between these two incisions by blunt dissection with scissors. A clamp was applied to the tissue thus raised, and the latter was freed from its lower attachment and

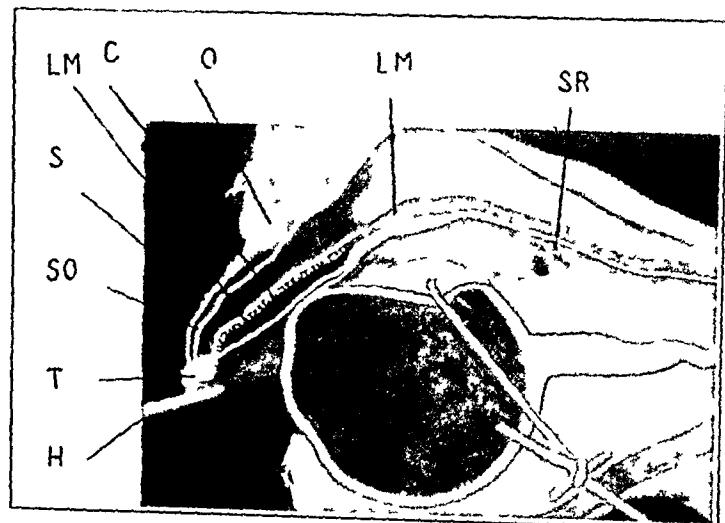


Fig 2.—Sagittal section through the orbit, showing that the tendon of the levator muscle and Muller's muscle (*LM*) are separated as one layer of tissue in the routine dissection involved in resection of the levator muscle (*LM*) through the conjunctiva (*C*). *H* indicates the hook, *T*, the tarsus, *S*, the skin, *O*, the orbicularis muscle, and *SR*, the superior rectus muscle (retouched photograph of a cadaver specimen).

dissected upward for 10 to 12 mm.⁴⁸ Three layers of tissue were thus separated—the conjunctiva, Muller's muscle and the pretarsal fascia. Pieces of colored celluloid were then inserted between these layers, so that a blue piece was placed between the conjunctiva and Muller's muscle, a red piece, between Muller's muscle and the pretarsal tissue and a green piece, between the pretarsal tissue and the skin. The entire orbit was then sectioned in the sagittal plane, and the fascial planes and the tissue layers

⁴⁷ In this dissection it was certain that Muller's muscle, which is always attached to the upper border of the tarsus, was dissected upward. But at the time it was not definitely determined whether the aponeurosis was also included.

⁴⁸ The tissue plane of this dissection seemed to be entirely in the plane of the orbicularis muscle.

were studied. From behind forward, the first layer of tissue was the conjunctiva, to which a few fibers of Muller's muscle were still attached (fig 2). The first plane of dissection, marked by blue celluloid, passed between Muller's muscle and the conjunctiva. The second layer of tissue, to which the tarsus was attached, was made up of Muller's muscle, behind, and the levator aponeurosis, in front. The second plane of dissection, marked by red celluloid, passed between the aponeurosis, behind, and the septum orbitale, in front. The third layer of tissue was made up of septum orbitale and orbicularis muscle. The third plane of dissection, marked by green celluloid, passed through the orbicularis muscle, with the skin in front and the septum orbitale behind.

From this experiment, performed under conditions simulating those present in the operating room during routine resection of the levator muscle through the conjunctiva, the following conclusions were drawn:

- 1 A natural plane of cleavage exists between Muller's muscle and the conjunctiva, making it easy to separate the two.

- 2 Muller's muscle and the tendon of the levator muscle are removed together as one layer and are not easily separated or identified under these conditions.

- 3 The "pretarsal" fascia, anterior to the tarsus, is the same as the posterior fascial sheath of the orbicularis muscle and becomes continuous with the septum orbitale above the tarsus.

EXPERIMENTAL RESECTIONS OF THE LEVATOR MUSCLE

To test these conclusions further under conditions simulating those present in the operating room, three types of operation for resection of the levator muscle were done on cadavers, and the orbits were later sectioned sagitally, to determine how much and what tissue was removed.

1 Resection of the Levator Muscle According to the Wheeler Technic.—The right orbit of a cadaver was subjected to resection of the levator muscle according to the technic practiced by Wheeler. The lid was everted by means of an Ehrhardt clamp. The conjunctiva was incised 1 to 2 mm above the upper border of the tarsus and dissected free from Muller's muscle for 10 to 12 mm. An incision was then made through the tarsus 1 to 2 mm from its upper border down to the pretarsal fascia. The excised tarsus was grasped with forceps, and the tissues attached were dissected upward from the orbicularis muscle for 10 to 12 mm. Three double-

armed silk sutures were passed through the conjunctiva near its cut edge and then through the attachments of the levator muscle 10 mm from the excised tarsus. The excised tissue was only 5 mm long in its relaxed state. The sutures were then passed through the cut edge of the tarsus and through the skin and tied over a rubber peg. The excised tissue was sent to the laboratory for histologic study and found to consist of tarsus, Muller's muscle and a connective tissue layer representing the tendon of the levator muscle. The orbit was then sectioned in the sagittal plane, and the tissues were studied grossly. This showed that less than one half of Muller's muscle and the tendon of the levator muscle had been removed (fig 3).

This procedure closely approximated that practiced routinely by the late Dr. Wheeler for

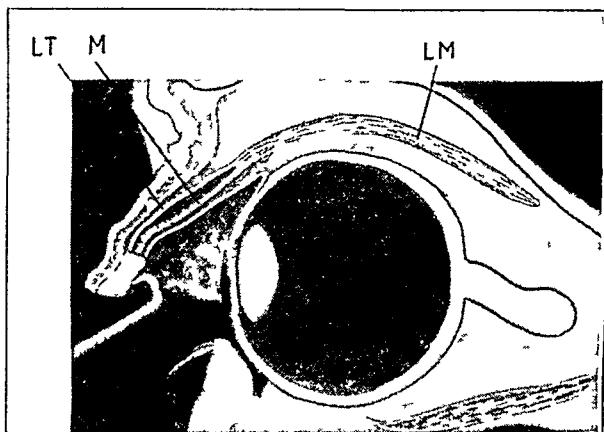


Fig 3.—Sagittal section through the orbit after routine resection of 10 mm of tissue of the levator muscle (LM) according to the Bowman-Wheeler technic. Note that only a small part of the tendon of the levator muscle (LT) and Muller's muscle (M) has been removed (retouched photograph of a cadaver specimen).

mild ptosis. It was obvious, from the small amount of tissue removed, about 5 mm, that undercorrection would result in the patient, having severe ptosis. In justice to the operation, it was decided to repeat the procedure on another cadaver, to determine whether this technic could be modified by simply removing more tissue of the levator muscle and thus make it useful for severe ptosis. Therefore resection of the levator muscle was done on another cadaver, according to the preceding technic except that instead of resecting what appeared to be 10 mm of the levator tissue, as was done the first time, an apparent 20 to 25 mm was removed. The excised tissue when relaxed measured only 18 mm in length⁴⁹ and was sent to the laboratory.

49 It was difficult to measure the excised tissue accurately because of its elasticity and lack of tone. If the tissue was stretched horizontally, it became shorter vertically, and vice versa.

for histologic study. The specimen consisted of a small part of the tarsus, a layer of Muller's muscle, most of the tendon of the levator muscle and a few striated muscle fibers from the levator muscle. The orbit was then sectioned in the sagittal plane, and the tissues were studied grossly (fig 4). Practically all of Muller's muscle and the aponeurosis of the levator muscle

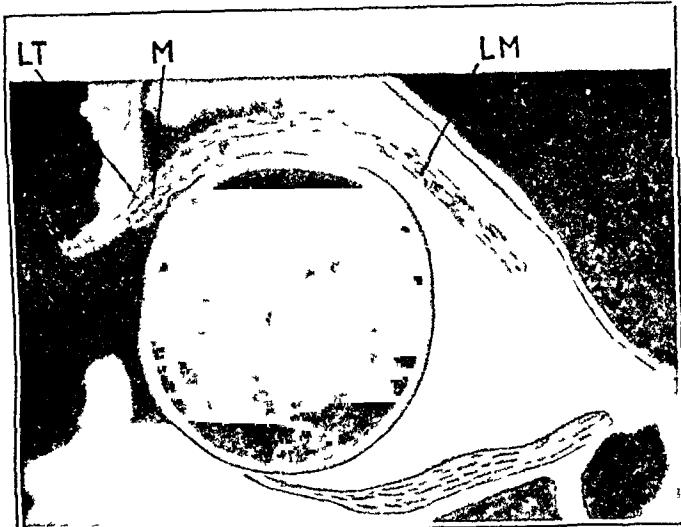


Fig 4.—Sagittal section through the orbit after resection of a large amount of the levator muscle (*LM*) according to the Bowman-Wheeler technic. Note that all but 2 or 3 mm of the tendon of the levator muscle (*LT*) and Muller's muscle (*M*) has been removed (retouched photograph from cadaver specimen)

muscle had been removed. The tissues excised consisted, therefore, of both Muller's muscle and the tendon of the levator muscle.

From this study it may be concluded that resection of Muller's muscle through the conjunctiva, according to the procedure just outlined, must include the tendon of the levator muscle as well as Muller's muscle, and that a natural plane of cleavage exists between Muller's muscle and the conjunctiva, on the one hand, and between the aponeurosis and the septum orbitale, on the other. It also demonstrates that one can, with effort, resect almost all the attachments of the levator muscle with this technic. Traction on the tissues of the levator muscle stretches them and gives an erroneous impression of how much tissue is being removed.

2 Resection of the Levator Muscle According to the Blaskovics Technic—A third cadaver was subjected to the Blaskovics procedure. The upper lid was everted by a Desmarres lid evertor, and an incision was made through the conjunctiva 3 to 4 mm from the upper border of the tarsus. The conjunctiva was freed from Muller's muscle, and three sutures were passed through the cut edge, to be used for traction. Three other sutures were then passed through Muller's muscle 3 to 4 mm from the tarsus and used for traction. The tissues attached to the up-

per border of the tarsus were cut across below the sutures and dissected free from the conjunctiva, on one side, and the pretarsal fascia, on the other, for 20 to 25 mm. During this procedure the lid evertor was removed and the upper lid retracted upward to give a better exposure. The upper half of the tarsus was now excised, and the three double-armed sutures in the conjunctiva were passed through the levator muscle 20 to 25 mm from its cut edge and left loose. Another set of double-armed silk sutures was then passed through the anterior surface of the levator muscle 5 to 6 mm above the line of the other sutures. The upper row of sutures was passed through the skin 5 to 6 mm from the border of the lid and left loose. The lower set of sutures was then passed between the tarsus and the orbicularis muscle and brought out through the skin 2 mm from the lashes. The upper set of sutures was tied over a rubber peg and cut off, while the lower set was tied without the use of a rubber peg. The excised tissue was sent to the laboratory for histologic study. The specimen consisted of Muller's muscle, the tendon of the levator muscle and a large part of the anterior end of the striated muscle fibers of the levator muscle. The orbit was then sectioned in the sagittal plane, and the tissues were

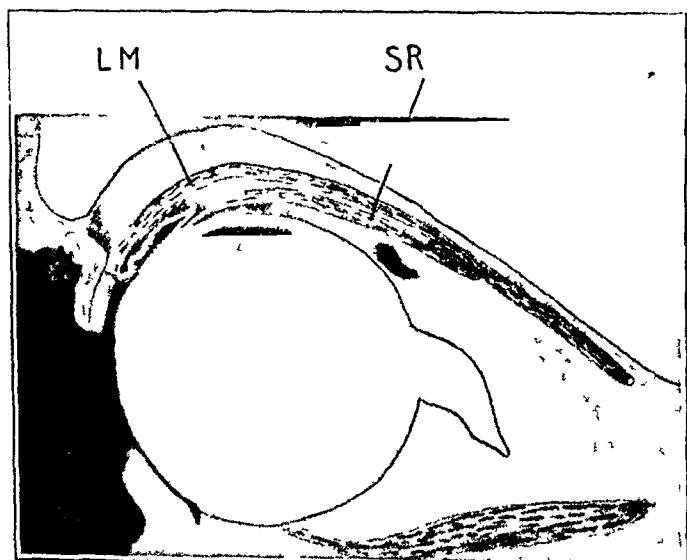


Fig 5.—Sagittal section through the orbit after resection of a large amount of the levator muscle according to the Blaskovics technic. Note that all of the tendon of the levator muscle and all of Muller's muscle have been removed (retouched photograph of a cadaver specimen)

studied grossly. Inspection showed that all of Muller's muscle and the aponeurosis had been excised and that the sutures had been placed in the anterior end of the striated muscle fibers of the levator muscle (fig 5).

This experiment shows that with the Blaskovics technic for resection of the levator muscle both Muller's muscle and the aponeurosis, as

well as part of the levator muscle itself, were resected.

3 Resection of the Levator Muscle Through the Skin.—The left orbit of a fourth cadaver was subjected to resection of the levator muscle through the skin. A lid clamp was inserted fair up into the upper fornix and an incision made through the skin 10 mm above the lashes. The skin was reflected upward and downward 4 to 5 mm and an incision made through the orbicularis muscle and the septum orbitale, exposing the orbital fat and the anterior surface of the aponeurosis of the levator muscle. A retaining speculum was inserted to hold the upper lip of the wound and the fat out of the way and to expose the attachment of the aponeurosis to the

above the lashes and tied over a rubber peg. The orbit was then sectioned in the sagittal plane, and the tissues were studied grossly. They showed that all of Muller's muscle and the aponeurosis of the levator muscle had been excised and that the sutures had been passed through the anterior end of the levator muscle (fig 6).

This experiment revealed that the aponeurosis of the levator muscle and Muller's muscle are resected together through the skin. Much better exposure is obtained when resection of the levator muscle is performed through the skin. Also, more muscle can be excised, the sutures more firmly anchored and more accurate closure effected. It is impossible to confuse Muller's muscle with the tendon of the levator muscle when the levator muscle is resected through the skin.

SUMMARY

Resection of the levator muscle is the operation of choice for the correction of ptosis when this muscle is not completely paralyzed. There are various surgical procedures for increasing the lifting power of the muscle. Inadequate correction of ptosis following resection of the levator muscle through the conjunctiva may be due to unintentional resection of Muller's muscle, instead of the tendon of the levator muscle. Anatomic studies of the upper lid and of the levator muscle in cadavers demonstrated that Muller's muscle is never resected alone but that the tendon of the levator muscle and Muller's muscle are always excised together as one layer in the routine resection of the levator muscle.

CONCLUSIONS

Under conditions simulating those in the operating room, Muller's muscle and the tendon of the levator muscle are always excised together in the routine resection of the levator muscle as done through the conjunctiva.

When resection of the levator muscle gives inadequate correction of ptosis, failure may be due to resection of Muller's muscle instead of the tendon of the levator muscle.

Inadequate correction of ptosis following resection of the levator muscle may be due to insufficient resection, pulling out of the suture or absence of the levator muscle.

Prof S R Detwiler, director of anatomy, Columbia University College of Physicians and Surgeons supplied the cadavers used in this study.

430 Union Street

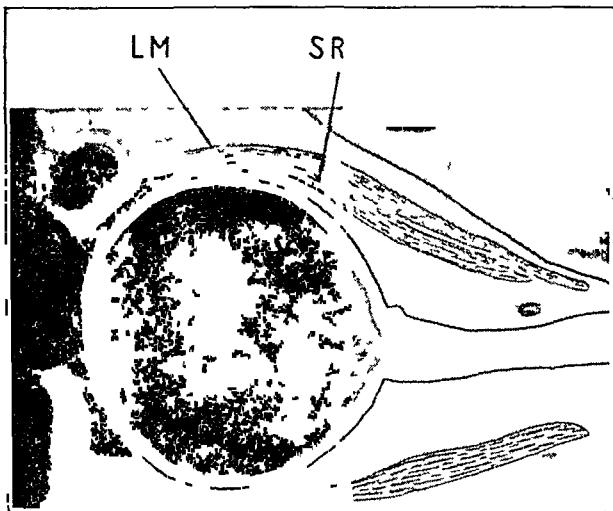


Fig 6.—Sagittal section through the orbit after resection of a large amount of the levator muscle (*LM*) done by the cutaneous route. Note that all of the tendon of the levator muscle and all of Muller's muscle have been removed. *SR* indicates the superior rectus muscle (retouched photograph of a cadaver specimen).

tarsus. The aponeurosis of the levator muscle and Muller's muscle were then dissected free from the underlying conjunctiva and reflected upward for a distance of 10 to 12 mm. A clamp was then placed on both the aponeurosis and Muller's muscle, and, while traction was exerted downward, the levator muscle was dissected free from the orbital fat, above, and the conjunctiva and Tenon's capsule, below. Three double-armed sutures were passed through the levator muscle from behind forward 15 to 20 mm from its lower edge, and the tissue anterior to the sutures was excised. The sutures were then passed through the upper border of the tarsus and out through the skin 8 to 10 mm

UVEITIS, WITH POLIOSIS, VITILIGO, ALOPECIA AND DYSACOUSIA (VOGT-KOYANAGI SYNDROME)

CAPTAIN EMANUEL ROSEN
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Bilateral uveitis associated with alopecia, poliosis, vitiligo and dysacusia has been described in ophthalmic literature 47 times. Recently the name Vogt-Koyanagi syndrome has been offered to supplant these harsh sounding terms,¹ and Martínez² has attempted to rename the syndrome Vogt-Harada disease. The latter suggestion has a further purpose than mere lingual torsion, for Martínez has tried to link the signs and symptoms of the more malignant Vogt-Koyanagi syndrome with those of the usually benign Harada disease. According to Babel's definition a case of nontraumatic bilateral uveitis accompanied by any or all of the associated signs—namely, poliosis, vitiligo, alopecia and dysacusia—should be regarded as an instance of the Vogt-Koyanagi syndrome.³ This definition has been accepted for the purposes of the present study.

It is known that the disease in question has a protracted course, responds poorly to treatment and usually terminates in partial or complete blindness. The purpose of this paper is to present a case of the disease, to draw some conclusions about its nature and course and to suggest a method of treatment.

REPORT OF A CASE

The patient, a Puerto Rican residing in New York, reported to the ophthalmologic clinic at the station hospital on Feb 25, 1943, complaining of blurred vision in both eyes. He desired a change in his glasses, which were six months old and which seemed never to have improved his vision much. The patient was 24 years old and had been in the United States for four years. He had been in the service only five months and believed his vision had gradually become worse during that time.

History—The patient's family history showed no record of any pigmentary, ocular or cutaneous disease. There was no family history of consanguinity. The

1 Babel, J., cited by Carrasquillo, H F Uveitis with Poliosis, Vitiligo, Alopecia and Dysacusia (Vogt-Koyanagi Syndrome), Arch Ophth 28 385 (Sept) 1942

2 Martínez, L, Jr An Soc mex de oftal y oto-rino-laring 16:273, 1941

3 Carrasquillo, H F Uveitis with Poliosis, Vitiligo, Alopecia and Dysacusia (Vogt-Koyanagi Syndrome), Arch Ophth 28 385 (Sept) 1942

patient's parents were both alive and well. The father, who was 60 years old, had had graying of the hair during the last four years. There were four brothers and three sisters. No member of the family had shown any evidence of alopecia, poliosis, dysacusia or vitiligo. There was no family history of tuberculosis, syphilis, diabetes, nephritis or mental or nervous disease. The patient did not recall any sudden vasomotor, neurotic, pigmentary or depigmentary phenomena in members of the family.

There had been no unusual circumstances attending the patient's birth. He said he had not had any childhood diseases other than chickenpox, measles and scarlet fever, these conditions having been rather mild and having produced no serious complications.

The patient had no recollection of having had malaria, typhoid or any "parasites". He had never had an abnormal reaction to a drug, serum or foreign protein. There had been no personal history of asthma, hay fever or other allergic manifestations, though two of his sisters had had asthma. He said also that he had not had any venereal disease, he gave no history of any generalized eruption or disturbance of the mucous membrane.

The patient had never been hospitalized for either a surgical or a medical ailment until the onset of the present disease of the eyes. In 1941, while riding a bicycle, he had become involved in an automobile accident, in which his left forearm and wrist were injured. There was no history of unconsciousness, the patient having been retained for only a few hours at the hospital.

The patient's difficulties with his eyes began in 1938, when he became aware of difficulty in reading newspapers and books. There was no difficulty for distant vision. There was no acute sudden onset, and there existed at no time any of the acute symptoms which usher in an acute febrile disease. At the time of onset of these ocular symptoms the patient was in Puerto Rico and was swimming under water a great deal. He believed this activity caused his eyes to become severely inflamed and to remain so for the greater part of the day. He consulted his family physician regarding this redness of his eyes. "Eye drops" and some form of internal medication were prescribed, and the patient was advised to continue this therapy for one month. At the end of this time no improvement was noticed, and the patient sought aid in San Juan, Puerto Rico, finally securing the services of an ophthalmologist, whose diagnosis was bilateral uveitis. Treatment was given accordingly, the patient making weekly visits to this physician for a total of six visits. During this period the patient was given a solution of drops to instil into his eyes three times daily, internal medication and hot compresses. No focal investigation was made further than to uncover and have removed seven infected teeth. A Wassermann test of the blood was reported as giving a negative reaction. On the fourth day after the original attack the patient noticed the appearance of white eye-

lashes Two white patches of hair, symmetrically located in the occipital area, appeared about this same time The vision rapidly diminished and was considerably reduced for distance perception The patient observed that if he directed his gaze toward the ceiling he was able to see the floor more clearly

After six weeks of treatment at San Juan vision was much improved, and the patient of his own accord discontinued medical care One year later there occurred a second attack, which was much more pronounced in the right than in the left eye No medical aid was sought on this occasion After several weeks his eyes again began to clear up, though not completely In the spring of 1942 the patient again noticed a gradual



Fig 1—Photograph of the patient's eyelids and brows, showing several white eyelashes

blurring of vision, which became progressive and appeared much more pronounced in the left eye This left eye became much worse during succeeding summer months In the autumn of 1942 the patient was seen at one of the clinics of the station hospital His glasses were changed, but there was no great improvement in his ability to read

In none of the four attacks which the patient described was the onset accompanied or introduced by any acute symptoms, such as nausea, vomiting, headache or fever At no time had there been pain of any sort—dizziness, tinnitus, deafness, lassitude, anorexia, stiffness of the neck or febrile reaction

Examination—The patient was a short, dark Puerto Rican, 5 feet 1 inch (155 cm) in height, weighing 128 pounds (58 Kg) and fairly well built He had thick hair, which was dark except in the region of the two occipital prominences, here there were some small symmetric patches of white hair There were some small white eyelashes on each of the lids (fig 1) Examination of the axillary and pubic regions failed to show any white hairs Sparseness of hair was noted on the temporal portion of each eyebrow

There was a mild papular eruption on the patient's forehead and on both malar regions Careful examination of the skin of the back, the shoulders, the chest and the arms showed several small depigmented islands, none of which was more than 10 mm in its greatest diameter, these islands were symmetric both in location and in appearance The vitiligo was present on the shoulders and the chest and was not visible elsewhere.

The results of otolaryngologic consultations were reported as follows The nose was essentially normal, the pharynx showed infected tonsils, the larynx was normal, and all the sinuses transilluminated readily

The wall of the left auditory canal and the left tympanic membrane were normal, whereas the right eardrum showed a scar on the membrane at 7 o'clock Weber and Rinne tests gave negative results An audiogram was taken and found normal

Examination of the teeth showed that several upper teeth were lacking All the remaining teeth were in good condition, with no indication of abscess or of involvement of the gums There was some slight recession of the gums

No abnormality was noticed as regards pigmentation of the breast The heart and the lungs were not remarkable

There were several white eyelashes in both the upper and lower lids A faint bilateral ciliary injection was present in each eye The pupils were equal but semi-dilated (5 mm, with a retarded and minimal reaction both to light and in accommodation but with some response) No abnormalities of muscle were noted There was nothing remarkable about the conjunctival surface of the lids or about the lacrimal apparatus The anterior chambers were rather deep Keratic precipitates were visible on the corneal surfaces with the ordinary loupe (fig 2) Some pigment was also present on the anterior capsule of each lens and became much more readily visible when the pupil was dilated The slightly different color of the inner circle of the iris was striking Many minute "fluffs" of exudate were seen encircling the pupillary margin, probably a

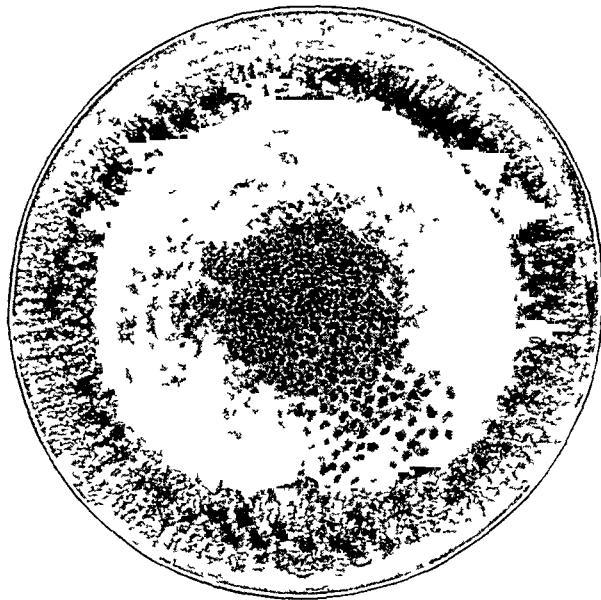


Fig 2—Drawing of the iris and the pupil of the patient's right eye

dozen of these flocculi being present within each pupillary circumference Between the flocculi was a thin area of exudate plastered on the capsule of the lens

One small posterior synechia was present in the right eye at 6 o'clock The vitreous appeared clear except for an occasional minute vitreous "floater"

Slit lamp studies of the cornea showed deposition of precipitates bilaterally The number was much greater in the left eye The keratic precipitates were not deposited in the triangular manner usually described for this condition but were for the most part crowded around the summit of the cornea The precipitates were made up of various-sized islands which en masse pro-

duced a disklike arrangement. The larger precipitates, which were pellucid and crenelated, were definitely non-pigmented but had a lardaceous consistency. The smaller deposits between the larger ones had slight pseudopods resembling melting ice. In the anterior chamber some fine dustlike grains could be seen moving slowly. The aqueous flare was pronounced. There was no real atrophy of the main structure of the iris, for diaphanoscopy did not allow the passage of light rays except at the pupillary border. The entire pupillary border of each eye had a moth-eaten appearance. None of the small accordion-like folds of this portion of the iris were visible. The "chewed-out" effect made the inner circle of the iris look much like a gray border in a brown iris. In the right eye at 6 o'clock there was

capsule of the lens in the zone of specular reflection a polychromatic luster was obtained. The reflex from the vitreous was not easily obtained, since the corneal precipitates were clustered closely about the central corneal area. When a narrow beam of light was played well into the anterior third of the vitreous, difficulty was encountered in bringing out the framework of the vitreous. There were two reasons for this difficulty. First, there was no absorption of rays of light by the pigment epithelium of the retina, so that the effect was like that seen in an albino; secondly, the framework of the vitreous was decomposed. The vitreous resembled that of a high myope, wherein the strands of the framework are brown and bare and the horizontal interfibrillar substance has disappeared. Within the

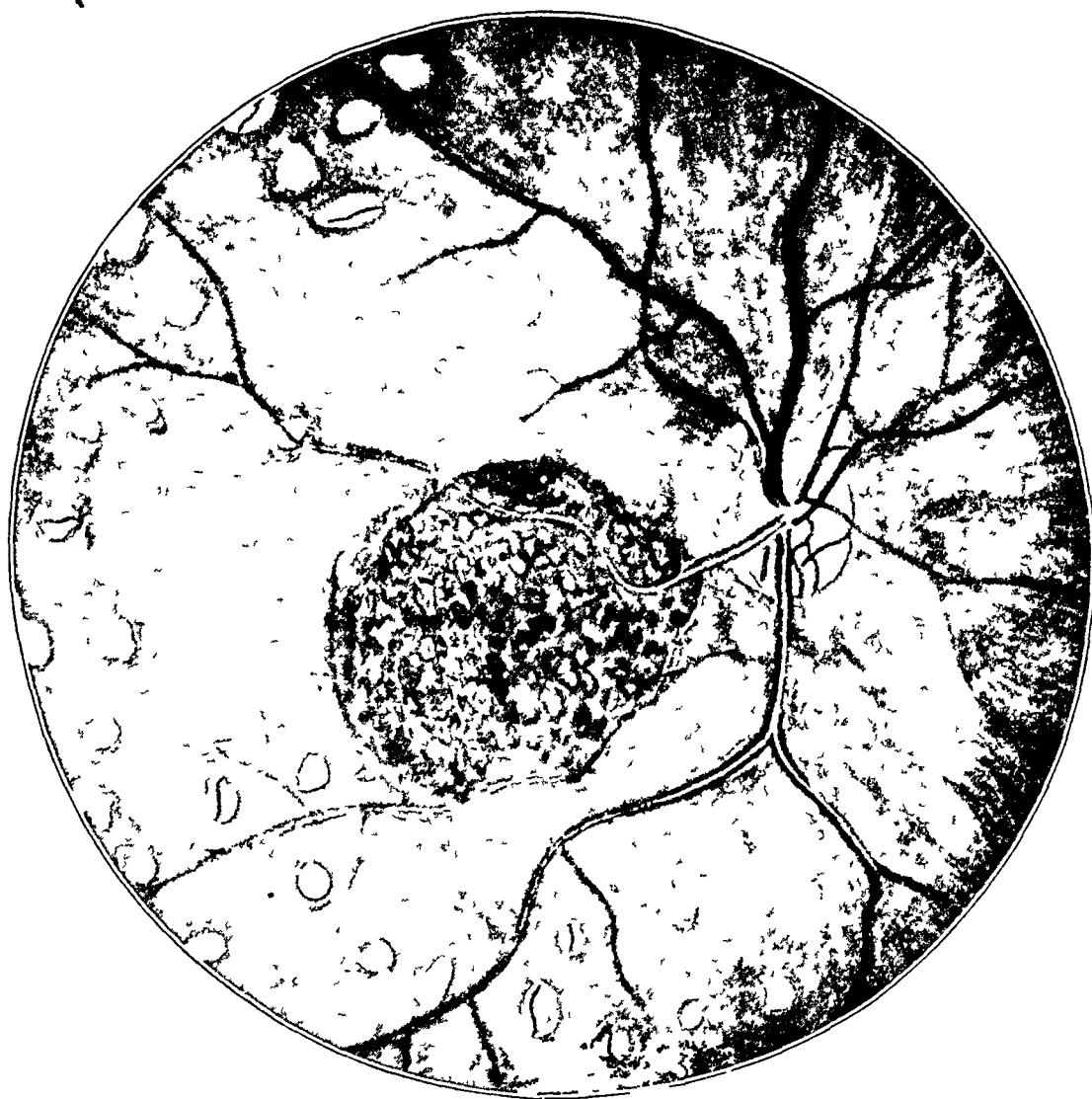


Fig. 3.—The fundus of the patient's eye

a peculiar synechia which folded down behind the iris to be attached to the capsule of the lens like a tree trunk with two large limbs growing out of the ground. The structure of the iris itself was not abundantly convoluted and suggested a primitive type of iris. The small flocculi seen with the ordinary loupe looked much more fluffy under the slit lamp, for they were translucent and resembled cotton balls. Some deposition of the pigment of the iris could be seen in these "fluffs," as well as in the exudate between them. There were also many minute granules of pigment on the anterior capsule of the lens, along with some rather solid-looking remnants of dense brown pigment. The lens appeared to be clear throughout, but when the focus was carefully directed on the part of the posterior

fluid clefts of the vitreous some minute brownish granules could be seen. In the right eye just a short distance behind the retrobulbar area was a definite fluid cleft resembling a small detachment of the vitreous. The generalized return "glow" of the illuminating beam masked a good many characteristics of the vitreous, but the thin, rootlike appearance seemed to be the predominant characteristic of the degeneration of the vitreous.

Of more than casual interest was the appearance of the eyegrounds, which were almost identical (fig. 3). The background of the fundus in each eye was a peculiar light orange color, giving off a glowing effect. Certain areas were reluctant, with the light passing through the eye proper as is seen in albinism. This

effect could be obtained from any part of the room, the light striking the fovea being directed back into the examiner's eye. No dilation of the pupil was required for the production of this phenomenon. In the right eye the nerve was elongated vertically and was rectangular rather than oval. It was somewhat less pink than normal, with a lack of marginal delineation which was due not to blurring of the disk but rather to depigmentation in the region of the retinal pigment at the papilla, so that the nerve head blended into the surrounding tissue. This effect was due to three scleral lesions surrounding the nerve head, which were actually regions of scleral atrophy. They were slightly whiter than the portion of the nerve head adjacent to them but blended harmoniously into the optic nerve with slight demarcation. The vessels at the disk were not unusual. The physiologic cup was invisible. In the macular region there were several round and oval slate-colored, pigmented lesions varying in size from $\frac{1}{8}$ to $\frac{1}{3}$ disk diameter. These were closely packed together, with some suggestion of overlapping. These lesions occupied an area equal to 3 or 4 disk diameters. Among the lesions were some retinal areas with a granular stippling, these areas appeared fairly normal.

When the periphery of each eyeground was scanned it was observed that the background of the fundus in the periphery was much darker than the paracentral zone. Scattered throughout the periphery in an incomplete girdle were many small grayish lesions which for the most part appeared to be old. These discrete lesions varied in size from $\frac{1}{8}$ to $\frac{1}{2}$ disk diameter. Many were gray-white and without a coating of pigment. Others contained pigment within their centers. There were minute lesions with rings of pigment. The larger grayish oval lesions had the long axis running in a horizontal direction. Through the structure of many the choroidal vessels were visible as a striking feature. Many of these foci were closely crowded and clustered into clumps of three or four. These appeared for the most part in a dirty, brownish gray background. There was a tendency toward coalescence of these patches.

Laboratory and Other Tests.—The blood chemistry was as follows: nonprotein nitrogen, 21 mg per hundred cubic centimeters; sugar, 95 mg; urea nitrogen, 10 mg; cholesterol, 160 mg; uric acid, 2 mg; globulin, normal. The sedimentation rate was 6. The Wassermann and Kahn reactions were negative.

Examination of the urine showed a specific gravity of 1.023. Analysis of the urine gave negative results for sugar and for albumin. The microscopic study showed an occasional epithelial cell, some mucous shreds and some crystals of calcium oxalate.

The spinal fluid was clear. It contained 3 leukocytes per high power field, all of which were lymphocytes. The sugar content of the spinal fluid was 62.5 mg per hundred cubic centimeters. There was no globulin. The Wassermann and Kahn reactions were negative with all dilutions. The colloidal gold curve was 1122210000.

Repeated tests for ova in feces disclosed the presence of *Trichuris trichiura*. Several tests for occult blood gave positive results at the same time.

The Mantoux test gave a strongly positive reaction after forty-eight hours, whereas the reaction to the Volmer patch test was negative.

Roentgenograms of the chest, the heart and the mediastinum were reported as showing no pathologic conditions. There was no evidence of hilar tuberculosis or of cardiac disturbance. The basal metabolic rate was +4 per cent.

On the initial examination, tension as measured by the Schiøtz tonometer was 17 in the right eye and 21 in the left.

Treatment and Course.—The usual instillation of atropine sulfate solution along with application of hot boric acid compresses was given three times daily to both eyes. Foreign protein in the form of boiled milk was given every forty-eight hours for six injections in gradually increasing doses, starting with 4 cc and working up to 10 cc. When the ova of *T. trichiura* were discovered in the stool an antihelminthic in the form of hexylresorcinol was prescribed, and several courses of therapy were outlined until successive examinations of stools failed to reveal the parasite.

The treatment for the Vogt-Koyanagi syndrome has been diversified, but since the cause is not known, most treatment has been given empirically and symptomatically. Salicylates, arsenicals, iodides, foreign proteins, tuberculin and uveal pigment have all been tried with no apparent success. Nakamura⁴ administered tuberculin in a case of Vogt-Koyanagi syndrome and believed he had a beneficial form of therapy, but his patient's final visual results were limited to the ability to see movements of the hand at 6 cm with each eye.

Verhoeff and Irvine⁵ in 1936 reported an effective treatment for sympathetic ophthalmitis. A series of 35 cases was reported in which diphtheria antitoxin was used, with good results when the patients were treated early. Some time later horse serum was substituted for the original diphtheria antitoxin. Having seen fairly good results from this type of therapy, I decided to try a similar form of treatment in this case of the Vogt-Koyanagi syndrome.

⁴ Nakamura, B., cited by Rados, A. Bilateral Uveitis with Associated Detachment of Retina, *Arch Ophth* **26** 543 (Oct) 1941, Bilateral Uveitis Associated with Detachment of the Retina (Harada's Disease), *ibid* **23** 534 (March) 1940.

⁵ Verhoeff, F. H., and Irvine, S. R. New York State J Med **36** 63, 1936.

The patient was referred to the department of allergy, where careful investigation was made into his history, with special emphasis on sensitivity to horse serum. The patient was tested with concentrated horse serum, and a 4 plus reaction was reported, with a 1:10 dilution a 1 plus reaction was obtained. It was decided to desensitize the patient to horse serum by giving gradually increasing doses, beginning with very small amounts, over a long period. This was done over a period of weeks with careful check on the systemic reaction, the amount of the dose being gradually built up to a strength from which a shock reaction might be expected. The doses and the recorded reactions were listed by the allergy department in chronologic order as follows:

5/5/43	0.1 cc of 1:10 dilution	No reaction
5/6/43	0.3 cc of 1:10 dilution	No reaction
5/7/43	0.5 cc of 1:10 dilution	No reaction
5/8/43	0.8 cc of 1:10 dilution	No reaction
5/9/43	0.1 cc of concentrated serum	No reaction
5/10/43	0.2 cc of concentrated serum	No reaction
5/11/43	0.35 cc of concentrated serum	No reaction
5/12/43	0.6 cc of concentrated serum	No reaction
5/13/43	1.0 cc of concentrated serum	No reaction
5/14/43	1.75 cc of concentrated serum	Severe local reaction
5/18/43	1.75 cc of concentrated serum	No reaction
5/21/43	2.0 cc of concentrated serum	No reaction
5/25/43	3.0 cc of concentrated serum	A little soreness
5/27/43	4.0 cc of concentrated serum	A little soreness
5/31/43	5.0 cc of concentrated serum	No reaction
6/3/43	5.0 cc of concentrated serum	No reaction
6/5/43	5.0 cc of concentrated serum	No reaction
6/7/43	5.0 cc of concentrated serum	No reaction
6/9/43	5.0 cc of concentrated serum	No reaction
6/11/43	5.0 cc of concentrated serum	No reaction
6/14/43	5.0 cc of concentrated serum	No reaction
6/16/43	6.0 cc of concentrated serum	No reaction
6/18/43	7.0 cc of concentrated serum	Patient became sick 2 hours after injection, he had dizziness, then nausea and lost his appetite for about 2 days
6/21/43	5 cc of concentrated serum	Some nausea rest of day
6/24/43	5 cc of concentrated serum	Some nausea rest of day
6/28/43	5 cc of concentrated serum	Some nausea rest of day
6/30/43	5 cc of concentrated serum	Some nausea rest of day
7/2/43	5 cc of concentrated serum	Some nausea rest of day

The patient's pupils had been dilated with atropine sulfate in 1 per cent solution and kept under the influence of the cycloplegic for several months. His vision constantly decreased, reaching 20/400 in the right eye and 20/800 in the left eye in about four weeks. At the same time the corneal precipitates showed a marked increase in number, size and area of distribution. The "fluffs" and exudates on the capsule of the lenses appeared more pronounced. The tension, determined on March 9, 1943, was 17 for the right eye and 21 for the left (Schiøtz). About eight weeks after hospitalization it was noted that the right eye which had originally had fewer keratic precipitates on the cornea, had now become much more involved, so that the

fundus was barely perceptible, whereas the left eye had begun to show some slight but definite improvement as regards both the number of keratic precipitates and the visual acuity. This observation was recorded when the amount of horse serum injected into the patient had reached 2 cc.

On May 10, 1943, in the patient's tenth week of hospitalization, it was noted that many new flocculi were visible on the inner circle of the iris of the right eye. Tension at that time was 18 (Schiøtz) in each eye, visual acuity was 20/800 in each eye.

On May 15, 1943 a severe reaction occurred locally from the injection of 2 cc of horse serum. The patient's arm became swollen, red and painful several hours after he received the serum. The other reactions abated in twenty-four hours, but the swelling did not disappear completely until five days later. At the time of the reaction there appeared to be even more "K.P.'s" on the cornea of the right eye. The inner circle of the iris took on a new appearance, being translucent, as in senile atrophy of the iris, rather than the normal dark color. The numerous flocculi were persistent. No change was noted in the left eye at this date. After a few days the patient was again given injections of horse serum in slowly graduated doses, and by June 1 he was receiving 5 cc without showing any serious reaction.

On June 16, 1943 it was noted that the keratic precipitates were still extremely numerous on the cornea of the right eye but that the left eye was continuing to clear up. Vision on this date was 20/400 in the right eye and 20/800 in the left, unimproved by glasses.

The patient had been desensitized to 6 cc of horse serum, and there had been no recurrence of the original alarming reaction. The eyes were reported as being about the same. On June 18, 1943 the patient was given 7.5 cc of horse serum. There followed within two hours a marked systemic reaction, which persisted for two days. There were dizziness, nausea and anorexia.

On July 1, 1943 it was noted that the right eye was beginning to respond to therapy, the corneal precipitates were becoming sparser, the fundus was beginning to be more visible and some of its distinctive characteristics could now be made out. The patient's vision was now much better 20/70 in the right eye and 20/100 in the left, unimproved by glasses. There were no flocculi on the iris.

The use of atropine was discontinued in August. By this time the patient's vision had

become much better. He was able to read newspaper type with each eye. The corneal precipitates were slowly melting away, few were now visible in the left eye under the slit lamp. Many were still present on the cornea of the right eye, but these had the appearance of ice rapidly dissolving.

By the early part of September the vision in the right eye had been corrected to 20/20 and that in the left eye to 20/25. Only an occasional precipitate could be seen on each cornea. The inner circle of the iris in each eye was atrophic. The eyegrounds were the same as originally described, no changes having taken place in that region during all these months of observation.

During this period of hospitalization the patient lost 3 pounds (1.35 Kg.). The hexyl-resorcinol medication was continued until May

these studies⁶ have shown that there is a decrease in the number of chromatophores of the choroid, which tend to be grouped in the outer layers of the choroid. The pigment epithelium of the retina also shows areas of absent and of increased grouping of pigment. This change gives the fundus a particularly light appearance. This feature is striking, since the syndrome occurs in darkly pigmented races.

3 Another notable feature of this case was the characteristic arrangement of the keratic precipitates. At the height of the uveitis these precipitates were for the most part in the mid-corneal zone, closely crowded together. There was no suggestion of a generalized distribution or of a specific triangular "base-down" arrangement on the cornea.

4 The occurrence of small, fluffy "Koeppen nodules" was another feature of the inflamma-

TABLE 1.—Results of Hematologic Examinations

Date	Red Blood Corpuscles	White Blood Corpuscles	Hemo globin	Mono cytes	Baso phils	Eosino phils	Myelo cytes	Juveniles	Stab	Seg	Lympho cytes
February 26	3,970,000	8,000	85%			10			3	48	33
March 3	5,050,000	7,100	85%	6		6			18	49	13
March 5	4,050,000	6,050	90%	14							
March 11	4,150,000	8,300	85%	6	1	11			7	49	25
March 17	4,700,000	8,850	95%	8		4			2	56	30
April 6		6,600	90%	3		2			1	68	26
April 27	3,920,000	6,450	85%	5		4			3	52	36
May 17	4,300,000	8,500	85%	13		5			4	54	24
May 24	4,300,000	6,900	90%	10		6			4	58	2
May 31	4,750,000	8,200	85%	11		2			5	60	22
June 14	4,490,000	6,100	90%	8		5			6	59	22
June 28	4,180,000	5,550	85%	7		7			6	58	22
July 16	4,710,000	8,100	95%	8		9				52	31
September 18	4,800,000	7,400	90%	7		3				66	24

Several examinations of stools that failed to reveal parasites were reported in May. The studies of the blood, however, showed persistent eosinophilia until September (table 1).

DISTINCTIVE OCULAR CHARACTERISTICS IN THIS CASE

There are several ocular characteristics in this case which appear to be rather distinctive and which deserve special consideration as regards the ocular phase of the syndrome.

1 The red reflex was seen from almost any angle when a beam of light struck the eye. The effect was much like that seen in an albino (external albinism). This phenomenon was a direct result of a second feature, namely,

2 The depigmentation of the fundus, which in turn led to the albinotic appearance of the eyeground (internal albinism). There are only 4 histologic reports of cases of this disease, but

tory phase of the syndrome, particularly when considered in association with the capsular exudation.

5 The atrophy of the inner circle of the iris in each eye is another point of special consideration, since the depigmentation of this area seems to be the most outstanding feature in the entire syndrome. In the 4 cases reported histologically little emphasis was placed on this atrophic inner circle of the iris. Matsuoka, after performing histologic studies, stated that the iris showed some thickening and some infiltration of round cells with partial destruction of the pigment epithelium. Ogawa⁷ noted some scar tissue in the iris, although infiltration of round cells was also observed.

When the iris was transilluminated in the present case, a perfect ring of light was perceived.

6 Matsuoka Acta Soc ophth japon 37:1339, 1933

7 Ogawa Acta Soc ophth japon 38:1005, 1934

through the inner circle of the area of the iris. This ring was not "scalloped," as in senile atrophy of the iris, nor was it "chewed out," as in heterochromic cyclitis. The small accordion-like nodular convolutions of the inner circle of the iris were completely depigmented. There was no elevation of this portion of the iris above the next, more peripheral, portion.

6 In the periphery of the retina in each eye were several atrophic spots which had certain features that seemed to make them unique. Most of these white atrophic patches were oval or egg shaped, the long axis running horizontally. The absence of bands of pigment around the patches was particularly interesting, even though in some lesions a ring of pigment might be present and though pigment might even be found within the exudate. Many of these oval pigmented exudates were crowded closely together within a field of dirty brown retina. The presence of deposits of pigment within the centers of the lesions and the absence of girdles of pigment appear to be one of the retinal features of this and allied conditions.

7 Reports by several authors of extremely deep anterior chambers were confirmed in this case. Apparently, however, the depth of the chamber was not due to any retraction of the diaphragm of the lens or of the iris nor was there any suggestion of posterior funneling of the pupil.

8 The nerve head in this case was also most unusual in appearance. It was elongated ovally, and because of several small areas of depigmentation just adjacent to it, it produced an almost oblong effect. These depigmented foci blended gradually into the nerve head, with only a slight border of separation. Not long ago, while this patient was under observation, another patient for whom a diagnosis of sympathetic ophthalmia had been made was examined. This patient had been under the care of Dr. A. C. Woods and stated that he had been treated with uveal pigment for several months. Vision had been improved from perception of light to 20/70 in each eye. On examining this patient's fundi, I saw so striking a resemblance between his eye grounds and those of the patient whose case is presented here that successive examinations of both patients' fundi were made. In both cases the nerve heads were oblong, the fundi were depigmented and the peripheries showed identical oval white patches without pigment. These white patches have been regarded as at least suggesting sympathetic choroiditis,⁸ while trauma as opposed to

nontrauma has been suggested as differentiating sympathetic disease from both the Vogt-Koyanagi syndrome and Harada's disease.

9 The picture of the macula also calls for emphasis, since its heaped-up arrangement, its appearance of recurrent deposition and its density would lead one to believe that little central vision could be obtained. Vision of 20/20 and 20/25 therefore seems extraordinary and proves the necessity of attempting refraction before formulating an opinion as to the cause of reduced vision. The appearance of this heaped-up pigment, which looked as if there had been one layer deposited after another is in line with the grouping of pigment seen in histologic sections in this and related conditions.

10 The appearance of the vitreous under the slit lamp, which unquestionably took its characteristics from the presence of uveitis in a depigmented choroid, has already been discussed as a phenomenon of special significance.

EXTRAOCULAR CHARACTERISTICS

As regards the extraocular manifestation of this syndrome, the associated signs have been thoroughly discussed by several authors⁹ and require no repetition except for some statistical and some individual observations. A review and a tabulation of the case reports will disclose the incidence of these associated signs (table 2).

ETIOLOGY OF THE VOGT-KOYANAGI SYNDROME

In reports of this syndrome etiology has occupied a large place in the various discussions. Syphilis and tuberculosis have both had their advocates as causes of the disease, but an analysis of the statistics fails to offer adequate support for incriminating either. An endocrine disturbance has been postulated because of the involvement of dermal, pilous and pigmentary structures. The role played by the endocrine system in the disturbance of pigment in Addison's disease, in the condition of the skin and the hair

9 (a) Parker, W. R. Am J Ophth **14** 577, 1931, Severe Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch Ophth **24** 439 (Sept.) 1940 (b) Rones, B. Uveitis and Dysacusia, Alopecia and Poliosis, Arch Ophth **7** 847 (June) 1932 (c) Vogt Klin Monatsbl f Augenh **44** 242, 1905 (d) Koyanagi, Y. Klin Monatsbl f Augenh **82** 194, 1929 (e) Davies, W. S. Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch Ophth **14** 239 (Aug.) 1935 (f) Hutchinson, J. Arch Surg., London **4** 357, 1892-1893 (g) Zenker, C. Klin Monatsbl f Augenh **102** 429, 1939 (h) Lund, S. Acta ophth **16** 414, 1938 (i) Wechsler, D. Arch Ophth **57** 393, 1928

⁸ Erdmann, P. Klin Monatsbl f Augenh **49** 129, 1911 Givner, I. Harada's Disease, Arch Ophth **30** 331 (Sept.) 1943

TABLE 2—Analysis of Cases of the Vogt-Koyanagi Syndrome

Case No	Author	Year Reported	Sex	Able	Dysconia	Vitiligo	Polliosis	Onset	Complication	Wassermann Test	Tuberous sclerosis	Vision
1 Volt	Gilbert, V	1906	Male	18	+?	—	+ 12 wk	?	Uveitis severe	?	—	4/200 3/200
2 Gilbert, V	1910	Male	38	Alopecia	No dysconia	—	+ 1 poliosis	—	K P, hyphema	—	—	6/12, 6/6
3 J rdmann	1911	Male	14	?	?	(+2 yr)	(+2 yr)	—	Night blindness, albinoid fundus, typical history	—	—	5/36, 5/12
4 J Komoto	1911	Female	33	(?)	—	+	(+ 3 wk)	Headache, dizziness	Choroiditis	?	?	6/12, 6/12
5 Koyanagi	1914	Male	31	+ 3 wk	+ 3 wk	—	+ 3 wk	vomiting, fever	Typical attack	—	?	6/36 finger counting 10 ft
6 Koyanagi	1914	Male	34	+ + 3 wk	+ + 3 wk	—	+ 3 wk	?	Typical attack	—	?	Finger counting 10 ft 6/24
7 Demaria	1917	Male	18	?	?	+ 3 yr	+ 1	Pain in eye	Cataracts	—	—	Light perception each eye
8 Demaria	1917	Female	39	—	(1 yr —)	+ (1 yr —)	(+ 1 yr)	—	Cataract	?	?	Light perception no light perception
9 Itoh	1918	Male	26	+ 6 wk	—	+	(+ 12)	Negative	Deep anterior chamber, secondary glaucoma	—	—	Finger counting 10 ft
10 Komoto	1918	Female	42	(+ 8)*	—	+	(+ 8)	Negative	Typical	+	?	Finger counting 15 ft
11 Komoto	1918	Male	32	(+ 12)	—	+	(+ 12)	Negative	Typical	+	?	Finger counting 6 ft, finger counting 6 ft
12 Ariyama	1919	Male	26	(+ 8)	Trinitus (AI)	—	(+ 8)	Cold and fever	Retinal detachment	—	?	Hand movements each eye
13 Hata and Harada	1919	Male	24	(+ 8)	(+ 1)	+	(+ 8)	Hendache, pains in joints	Typical	—	?	Hand movements each eye
14 Komoto	1920	Female	31	(+ 6)	(+ 1)	+	(+ 8)	Hendache	Typical	?	?	0 2, 0 3
15 Komoto	1920	Female	31	(+ 12)	—	—	(+ 12)	Negative	Typical	—	?	0 3, 0 3
16 Baldino	1920	Male	25	—	—	(+ 1 yr)	(+ 1 yr)	Hendache	Typical	+	?	Hand movements each eye
17 Maseda	1920	Male	47	(+ 6)	—	+	(+ 6)	Pain in eye	Typical	—	?	Finger counting 6 ft
18 Wenzler	1928	Male	45	—	—	(+ 15 yr)	(+ 15 yr)	Severe headaches	Typical	—	?	Finger counting 10 ft later 20/15 in each eye
19 Koyanagi	1929	Male	40	(+ 3)	(+ 1)	(+ 1)	(+ 12)	Negative	Type II	—	?	20/200, hand movements
20 Koyanagi	1929	Female	34	(+ 12)	(+ 1)	(+ 1)	(+ 14)	Headache, cold	Typical	—	?	Light perception each eye
21 Koyanagi	1929	Male	34	(+ 6)	(+ 1)	(+ 1)	(+ 12)	Headache, sleepiness	Retinal detachment	—	?	Finger counting 6 ft
22 Koyanagi	1929	Female	40	(+ 1)	(+ 1)	(+ 1)	(+ 12)	Headache	Typical	—	?	Finger counting 12 ft
23 Kuhmann	1929	Female	30	—	(+ 16)	(+ 16)	(+ 16)	Headache dizziness	Typical	—	?	Light perception

* The numbers in parentheses represent the number of weeks after onset.

24	Gilbert	1930	Female	62	-	-	+ (?)	-	Typical	-	?	?	?	?
25	Gilbert	1930	Female	10?	-	-	+ (?)	-	Typical	-	?	?	?	?
26	Fialho	1930	Male	13	(+ 16)	-	?	(+ 16)	Typical	-	-	-	-	-
27	Parker	1931	Male	18	(+ 11)	-	(+ 6)	(+ 10)	Pain in eyes, photophobia, dimness V A	Typical	-	-	-	Finger counting 3 ft each eye
28	Parker	1931	Female	25	(+ 12)	Tinnitus (+ 2)	-	(+ 12)	Vertigo	Typical	-	-	-	Hand movements
29	Westkamp	1932	Male	34	(+ 8)	(+ 1)	-	(+ 8)	Headache, shock	Retinal detachment	?	?	Light perception	
30	Rones	1932	Male	10	-	-	(+ 4)	(+ 8)	-	Typical	(+ visual pigment)	Blind both eyes		
31	Rones	1932	Female	28	(+ 16)	(+ 16)	-	(+ 16)	Pain in eyes	Cataract	(- visual pigment)	Blind		
32	Avalos	1932	Female	42	-	-	(+ 16)	(+ 8)	Headache, vertigo, vomiting	Cataract, glaucoma	1+	?	Blind	
33	Nakamura	1932	Female	28	(+ 10)	(+ 2)	-	-	Headache, pain in eyes	Cataract, glaucoma	1+	?	Blind	Finger counting 6 in
34	Avalos	1932	Female	34	(+ 16)	(+ 2)	-	(+ 16)	Earache, headache, pain in eyes	Cataract, glaucoma	1+	?	Blind	
35	Jess	1933	Female	13	-	-	+ ?	(+ 16)	-	Adinosogenital dys trophy, cataract	?	-	Light perception	
36	Davies	1935	Male	31	(+ 6)	(+ 4)	-	(+ 6)	Headache and lethargy	Fundus, no details	?	-	Light perception	
37	Krasnoff	1935	Male	12	-	?	+ ?	+ ?	?	Typical	+	+	? Very poor	
38	Anastasi	1936	Male	16	-	-	•	+ ?	Acute articular rheumatism	Typical	-	-	Finger counting, 1/10	
39	Luo	1936	Male	31	(+ 3)	Tinnitus (+ 4)	•	+	Headache, vertex, earache	Glaucoma	-	-	Light perception	
40	Avalos	1936	Female	27	+	?	+ ?	+ ?	Pain in eyes	Typical	?	?	Blind	
41	Yanes Ferrer	1938	Female	46	(+ 8)	(+ 1)	-	(+ 8)	Vertigo, malaise	Phthisis bulbi	-	+1	Light perception	
42	Yanes Ferrer	1938	Female	35	(+ 8)	(+ 1)	(+ 8)	(+ 8)	Vomiting	Typical	-	-	20/30, 20/30	
43	Babel	1939	Female	52	-	-	(- 12 yr)	(+ 8)	Pain in eyes	Typical	-	-	5/30, 5/15	
44	Zentmayer	1941	Female	30	-	(+ 1)	+ ?	(+ 1)	Headache, eye pressure	Retinal detachment	-	-	Hand movements	
45	Carrasquillo	1941	Male	36	(+ 12)	(+ 6)	(+ 14)	(+ 12)	Malaise, headache, nausea and vomiting	Cataract	3+(U P neg)	+ + +	Finger counting 3 ft finger counting 3 ft	
46	Martinez	1941	Female	20	(+ 6)	(+ 2)	-	(+ 6)	Acute iritis	-	-	-	Light perception each eye	
47	Campos	1942	Female	34	(12)	(14)	-	(13)	Usual acute onset	Glaucoma (16% cosmo philia)	-	-	Light perception each eye	

in eunuchs and in the occasional relationship of exudative choroiditis in women to ovarian dysfunction has been pointed out.

The possibility of a vitamin deficiency disease¹⁰ has received little thought and less investigation. In some studies isolated features of the syndrome have occurred, such as the grayness of hair and the loss of cilia. Some form of vitamin therapy has been used in recently reported cases, with no significant response being observed.¹¹

The possibility of a virus infection as an important cause was early suggested by Gilbert,^{10a} who thought that the herpes virus played some part in his first case. The South American authors,¹² primarily because at the onset of the disease symptoms suggestive of cerebral involvement are present, considered that a virus infection produces a benign lymphocytic meningitis and an associated uveal involvement. Rubino^{11b} expressed the opinion that the condition is uveo-meningitis due to a virus with special uveo-meningotropism and also with specific melanotropism, which accounts for the pigmentary phenomenon.

In 1 case reported by Avalos^{12d} a cerebral decompression was performed because of suspected increased intracranial pressure. Yanes and Ferrer^{12c} expressed the view that in 1 of their cases there was roentgenologic evidence of increased intracranial pressure. These authors also favored the theory that the syndrome is caused by a virus. They cited experiments in which the virus of herpes febrilis was injected into the anterior chamber of a rabbit, producing depigmentation of the iris.

Because of clinical and histologic resemblance to sympathetic ophthalmia and because of the allergic theory offered to explain sympathetic ophthalmia, a similar etiologic relationship has been postulated for the Vogt-Koyanagi syndrome. Cramer¹³ attempted to explain some of the systemic signs accompanying the Vogt-Koyanagi syndrome on the basis of Elschnig's original allergic theory offered for sympathetic

uveitis. This theory is, of course, open to question, especially in view of the lack of experimental proof.¹⁴

Peters¹⁵ and Koyanagi have discussed the allergic role on which this syndrome may depend. Weskamp¹⁶ believed that liberation through destruction of uveal pigment could produce an antigen which might call forth an anaphylactic process. Antibodies possessing lytic power over pigmentary structures could then be formed.

The experiments of Riehm¹⁷ from 1928 to 1930 are of extreme and special interest in a consideration of the cause of this syndrome. This author showed that foreign protein injected into the eyes of a rabbit produced sensitizing reactions in the fellow eye only when the rabbit was pigmented and not when it was an albino. The importance of this finding is realized only when it is recalled that the Vogt-Koyanagi syndrome always occurs in darkly pigmented persons, the disease being limited to the darkly pigmented races. Some recent work by experimenters with albino and with pigmented rabbits seems to indicate that Riehm's observations were inclusive, but these same authors appear to give somewhat inconclusive proof for their deductions.¹⁸

Although the extensive experimental work of Woods¹⁹ and his associates has not been completely confirmed, there is much to indicate that allergy plays an important part in causing sympathetic uveitis. Sensitivity to uveal pigment, as manifested in cutaneous tests, has been tried in only 4 instances of the Vogt-Koyanagi syndrome; in only 1 was there a positive reaction to the tests. In the remaining 3 tests the negative reactions were explained by the fact that the disease had continued long enough in the patient for desensitization to occur. A study of the skin at the site of the injection of uveal pigment has shown a definite cutaneous response, slight in vascularity but marked in cellular

14 (a) Gilbert, W. *Klin Monatsbl f Augenh* **48** 24, 1910, 85-65, 1930, cited by Carrasquillo³ (b) Krasnoff *Zentralbl f d ges Ophth* **37** 121, 1937 (c) Jess Ber u d Versamml d deutsch ophth Gesellsch **49** 469, 1932

15 Peters, A. A. *Klin Monatsbl f Augenh* **50** 433, 1912

16 Weskamp, R. L. *Arch de oftal de Buenos Aires* **7** 728, 1932

17 Riehm, W. *Klin Monatsbl f Augenh* **81** 867, 1928, **90** 477, 1933

18 Schlaegel, T. F., Jr. *Am J Ophth* **27** 137, 1944

19 Woods, A. C. *New York State J Med* **36** 67, 1936, in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, London, Butterworth & Co., Ltd., 1940

11 (a) Martinez² (b) Rubino, A. *Ophthalmologica* **101** 321, 1941 (c) Campos, E. *Hospital, Rio de Janeiro* **22** 113, 1942

12 (a) Rubino^{11b} (b) Campos^{11c} (c) Yanes T. R., and Ferrer, O. *Rev cubana de oto-neuro-oftal* **7** 5 1938 (d) Avalos, E. *ibid* **1** 242, 1932, cited by Martinez² (e) Koyanagi^{9d}

13 Cramer, E. *Klin Monatsbl f Augenh* **51** 205, 1913

activity, which is unquestionably identical in histologic appearance with the picture of sympathetic uveitis.²⁰ It is conceded that the development of pigmentary allergy is not the sole cause and that some other factor is essential, such as the introduction of a virus which through the meninges eventually reaches the choroid. This may be the spark necessary to ignite an allergic phenomenon in an unusual soil. In the treatment of postoperative and post-traumatic uveitis (proved histologically to be nonsympathetic), Woods has been able to desensitize with uveal pigment patients who were sensitive to the uveal pigment tests and to produce complete arrest of the uveitis. Analysis of all reported cases shows that 20 patients had some form of cephalgia at the onset, and it is possible that in other patients this condition was not observed or evaluated. If some acute onset could be established in all cases and if studies of the spinal fluid could be made at the incipiency of the disease, the spinal fluid might yield the essential factor necessary to complete the cycle, notwithstanding Koyanagi's statement that the spinal fluid is never under pressure and yields no etiologic factor on investigation. Should the pia-arachnoid be the seat of original involvement and should there be extension to the choroid from this embryologically related membrane, the nature of the onset of the disease might be readily understood. Once dispersion of the uveal pigment had occurred, the subsequent anaphylaxis could well be established. The experiments of Takahashi²¹ and Tagami²² bear out these suppositions, for these authors by injection of cerebrospinal fluid, vitreous, subretinal fluid and other substances from patients with Harada's disease reproduced this clinical entity in rabbits, with histologic verification, or at least simulation, of sympathetic ophthalmia.

RELATION TO HARADA'S DISEASE

That this disease and Harada's disease are related entities cannot be doubted. There have been attempts to place the two diseases in one group,²³ and other attempts to classify the syndromes into single entities.^{14a}

20 Friedenwald, J S Am J Ophth **17** 1008, 1934

21 Takahashi, M Acta Soc ophth japon **35** 114, 1931 Okamura ibid **41** 679, 1937, **42** 196, 1938, cited by Rados¹

22 Tagami Acta Soc ophth japon **35** 114, 1931

23 Rubino^{11b} Martínez² Magitot, A., and Dubois-Poulsen, A Ann d'ocul **177** 145, 1940 Avalos^{12d} Koti and Kotsuki, cited by Rados^{14a} Duke-Elder, W S Textbook of Ophthalmology, St Louis, C V Mosby Company, 1941, vol 3

Both Rados and Koyanagi stated that with uveitis, poliosis and alopecia there is no formation of cataracts and that the presence of cataract is a point in favor of the condition's really being Harada's disease. In Carrasquillo's analysis³ of 29 cases 7 cases were reviewed in which complicated cataract was listed.²⁴ In Koyanagi's series (16 cases) there were no complicated cataracts. Rados also states that when retinal detachment occurs with nontraumatic bilateral uveitis the syndrome is specifically Harada's disease, in which "alopecia and poliosis do not figure as an integral part." Again, an analysis of all reported cases reveals that there were 5 instances of the Vogt-Koyanagi syndrome in which retinal detachment occurred.²⁵ Poliosis and alopecia were present in 4 of these cases.

Analysis of the entire series of cases of the Vogt-Koyanagi syndrome certainly indicates that many features which are supposedly pathognomonic for Harada's disease are present in the Vogt-Koyanagi syndrome. These features actually bridge the gap between the two diseases and probably represent different degrees of involvement in persons of variable sensitivity, the final pictures being similar. Among these features are complicated cataract, retinal detachment and depigmentation. It would therefore seem plausible that in one condition an immunity is soon developed to a severe allergic reaction (Harada's disease), whereas in the second condition the allergic process is much less acute, with the immune response almost nonexistent except when stimulated.

A summary of the tabulated case reports reveals the following facts (table 2)

Sex incidence was almost equal. There were 23 males and 24 females.

The youngest patient was 10 years old, the oldest patient was 52 years old, most patients were between 20 and 40 years of age.

Alopecia occurred in 31 of 40 recorded cases—a percentage of 73. There was no record concerning it in 7 cases.

Poliosis occurred in 43 of 47 cases—a percentage of 90. Records of 4 cases failed to include this sign.

Vitiligo occurred in 30 of 47 cases—a percentage of 63.

24 Rones^{9b} Avalos^{12d} Carrasquillo³ Jess^{10c} Demaria Arch de oftal hispano-am **17** 355, 1917

25 Weskamp¹⁶ Koyanagi^{9d} Nakamura⁴ Zentmayer, W Severe Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch Ophth **27** 342 (Feb) 1942 Arisawa Nippon Ganka Zasshi **23** 700, 1919, cited by Koyanagi^{9d}

Dysacusia was recorded in 24 of 44 cases—a percentage of 54

Cephalgic symptoms were present in 21 cases, pain in the eyes in 11, dizziness in 6, vomiting in 4, lethargy in 2, articular pain in 2 and earache in 1

As regards sequelae and complications, cataract occurred in 7 cases, glaucoma in 5, retinal detachment in 5 and a typical malignant tumor in 32. Endocrine dysfunction was present in 5

Reactions to the Wassermann test were positive in 7 cases, negative in 31 and unknown in 9. The Mantoux test elicited positive reactions in 4 cases, negative in 17 and undetermined in 26. Thirty patients had vision of 3/200 or less in each eye. Only 7 patients had vision better than

20/50 in only one eye. Uveal pigment was used only a limited number of times

SUMMARY

This report emphasizes the ocular rather than the extraocular features of this syndrome, although the extraocular features are tabulated, reviewed and listed. The incidence of each of the pathognomonic signs of the syndrome is given, all cases presented in the available literature being reviewed.²⁶

Horse serum is suggested as a form of therapy.

The relationship between this syndrome and other diseases is pointed out, and an explanation of the nature of the syndrome is suggested.

²⁶ T. H. Luo in the *Chinese Medical Journal* (50, 1409, 1936) referred to 10 cases in Japanese literature which were mentioned to him by Koyanagi, but Luo's reference to the Japanese literature is not correct.

MERIDIONAL ANISEIKONIA AT OBLIQUE AXES

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Many patients experience difficulties in wearing astigmatic corrections. Primarily, asthenopic symptoms are reported, but annoying distortions of objects in space are also mentioned. As a rule, the spatial distortions disappear in a short time when the correction is worn constantly. The asthenopic symptoms, on the other hand, may persist and even be so severe as to force the patient to abandon the glasses altogether. This is particularly true when the axes of the required cylinders are oblique.

The ocular discomfort has been attributed to the distortion of the retinal images produced by the cylindric spectacle lenses. These distortions have their principal effect in binocular vision. At an early date Wadsworth,¹ Culbertson² (who tried to correct the spatial distortion by rotating the cylinders) and Lippincott³ described some of the changes in the position and form of objects caused by astigmatic corrections. However, they did not explain the phenomena correctly. Green⁴ showed that the same effects could be obtained by using unequal figures in the stereoscope and concluded correctly that the phenomena were due to the stereoscopic interpretation of a changed relationship between the retinal images resulting from the cylindric spectacle correction. Friedenwald,⁵ Koller⁶ and, again,

From the Dartmouth Eye Institute, Dartmouth Medical School

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1 Wadsworth, O F On the Effect of a Cylindrical Lens, with Vertical Axis Placed Before One Eye, *Tr Am Ophth Soc* **2** 342, 1879

2 Culbertson, H Binocular Astigmatism, *J A M A* **11** 622 (Nov 3) 1888, *Am J Ophth* **5** 117, 1888

3 Lippincott, J A On the Binocular Metamorphopsia Produced by Correcting Glasses, *Arch Ophth* **18** 18, 1889

4 Green, J On Certain Stereoscopic Illusions Evoked by Prismatic and Cylindrical Glasses, *Tr Am Ophth Soc* **5** 449, 1888-1890

5 Friedenwald, H Binocular Metamorphopsia Produced by Correcting Glasses, *Arch Ophth* **21** 204, 1892

6 Koller, C Ueber eine eigenartliche Sorte dioptrischer Bilder Ein Beitrag zur Theorie der Cylinderlinsen, *Arch f Ophth* **32** (pt 3) 169, 1886, The Form of Retinal Images in the Astigmatic Eye, *Tr Am Ophth Soc* **6** 425, 1892

although later, Lippincott⁷ expressed agreement with this. Lippincott even suggested the use of these phenomena as a test for stereoscopic vision.⁸ In this test the subject would be asked to describe the apparent form of an object when viewed through a weak cylindric lens placed before one eye.

The distortion produced by a cylindric lens—or, for that matter, a meridional magnifying size lens—is an elongation of the image in the meridian of power, or magnification. Associated with that elongation are small rotary displacements of the

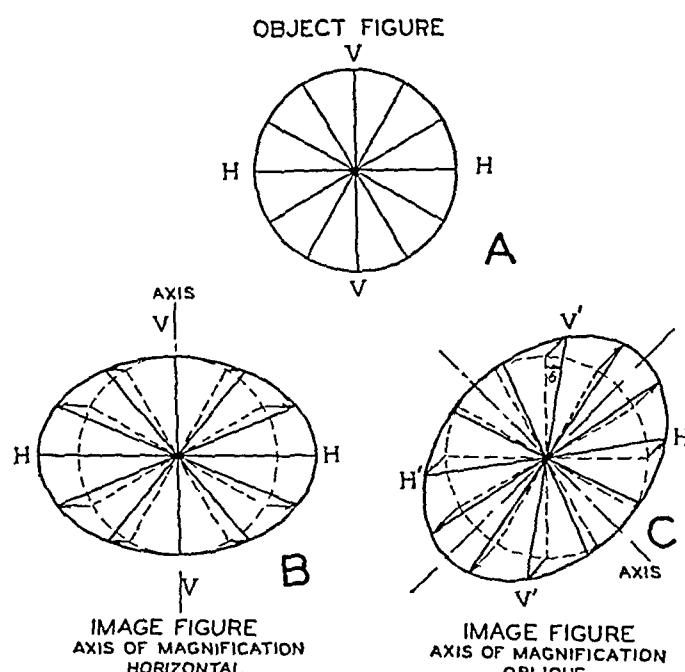


Fig 1.—An illustration of the distortion of a wheel-like figure (A) when observed through a cylindric lens, (B) when the axis is vertical and (C) when the axis is oblique. A rotary deviation of the images of vertical lines occurs when the axis is oblique.

images of all lines in space not parallel with or perpendicular to the axis of the lens. Figure 1 illustrates this fact. The image of a circular object (fig 1A), a wagon wheel for example, becomes an elliptic figure. Owing to the rotary displacements, the images of the spokes will no longer be spaced equally but will be crowded toward the meridian of elongation (magnification).

7 Lippincott, J A On the Binocular Metamorphopsia Produced by Optical Means, *Arch Ophth* **46** 397, 1917

8 Lippincott, J A New Tests for Binocular Vision, *Tr Am Ophth Soc* **5** 560, 1888-1890

If a cylindric spectacle lens is placed before one eye, with axis vertical (fig 1B), the elongation of the image will be in the horizontal meridian. The change in the disparities of the retinal images of the two eyes for all objects in space will be wholly in the horizontal meridian, and the spatial distortion will be symmetric above and below the visual plane. The small rotary deviations of the images will not cause additional stereoscopic spatial distortion. If the axis of the cylindric lens is oblique (fig 1C), the meridian of magnification is also oblique, and there will be changes in the disparities of the images in the two eyes both horizontally and vertically, these disparities increasing above and below the visual plane. They will introduce small rotary deviations in the images of vertical objects, and the result will be a distinct stereoscopic spatial distortion. This stereoscopic effect is the same as the one obtained in the stereoscope when two vertical lines, one seen by each eye, are fused. If these two lines are rotated slightly to converge at the top, the fused image appears to be a line inclined in space, nearer the observer at the top, if the two lines diverge at the top, the fused image appears to be tipped away from the observer at the top. In other words, whenever there is a deviation from parallelism between the images of a vertical line in the two eyes, that line will appear to be inclined with the top toward or away from the observer. We have designated the rotary deviation between the retinal images of the two eyes producing this stereoscopic effect as the declination error,⁹ following and extending the terminology introduced by Stevens.¹⁰

Declination errors can be produced by optical means, as has just been shown by placing cylindric lenses at oblique axes in front of the eyes. They can also be produced by a torsion of the two eyeballs, relative to each other, about the visual axes. When introduced optically, the declination error varies for the different meridians of the retinal image, the maximum occurring when the meridian of power is 45 or 135 degrees (fig 1C). If due to a cyclophoria, the declination error is the same for all meridians of the retinal images. Torsions of the eyeballs, therefore, cannot correct the declination errors produced optically. They could correct the error only in one meridian. Finally, declination errors may result if there is a basic meridional anisei-

konia at oblique axes not due to the correction of astigmatic refractive errors.

Declination, as a possible cause of asthenopic symptoms,¹¹ at one time were much discussed in the American ophthalmologic literature. Controversy developed about this point and about the relation of the declinations to cyclophoria and the part played by the oblique muscles of the eyes in correcting them.

But the discussion had no practical consequences, and interest in the subject soon waned. In more recent times the problem has been given little, if any, clinical attention. However, when it is mentioned, it is generally implied that spatial distortions can be the seat of ocular discomfort. Wolffberg,¹² for example, cited a number of cases in which patients reported annoying distortions of their surroundings and were unable to wear corrections for their astigmatism in spite of prolonged attempts. For most of these patients the axis of astigmatism was oblique. Erggelet¹³ recognized the problem and described and interpreted it correctly. He, too, pointed out that some patients with high cylindric corrections at oblique axes would rather put up with the lowered visual acuity than wear the cylindric lens. But he could offer no suggestion as to how the distortions could be avoided. He stated, however, that the spectacle wearer may learn how to reinterpret the visual impressions and how to disregard the distortions. This is sometimes made easier if the cylindric lenses are first placed in the horizontal or the vertical meridian and are then, over a period of weeks, slowly turned to the proper axis.

No solution has yet been found for the problem of the distortions arising in binocular vision from the wearing of cylindric spectacle lenses at oblique axes and the discomfort experienced by the patient. The reason is that the problem was not approached from the proper viewpoint. The declination errors at once become accessible to measurement and correction when they are recognized as being an aspect of aniseikonia.

Whenever ametropias of refractive origin of different amounts in the two eyes are corrected

¹¹ Eaton, F. B. The Physiology of Certain Oculo-Motor Phenomena with Respect to Some Recent Theories of Asthenopia, *J. A. M. A.* **23** 329 (Sept 1) 1894
Howe, L. The Muscles of the Eye, New York, Putnam's Sons, 1907, vol 2, pp 264 and 364
Savage, G. C. Ophthalmic Myology, ed 2, Nashville, Tenn, 1911

¹² Wolffberg. Störung des perspektivischen Sehens durch binokular korrigierende Zylindergläser, *Central-Ztg f Optik* **35** 10 and 20, 1914

¹³ Erggelet, H. Die Refraktion und die Akkommodation mit ihren Störungen, in Schieck, F., and Brückner, A. Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol 2, p 673

⁹ Ogle, K. N., and Madigan, L. F. Astigmatism at Oblique Axes and Binocular Stereoscopic Spatial Localization, *Arch Ophth* **33** 116 (Feb) 1945

¹⁰ Stevens, G. T. A Treatise on the Motor Apparatus of the Eye, Philadelphia, F. A. Davis Company, 1906

by glasses, an aniseikonic error may be expected¹⁴ Thus, the correction of unequal or unsymmetric astigmatism would theoretically result in a meridional aniseikonic error.

The correctness of this assumption has been borne out by innumerable measurements with the standard eikonometer in cases of astigmatic anisometropias in the horizontal and vertical meridians. Until recently there was no instrumentation which would permit an easy determination of the amount of aniseikonia in oblique meridians. This problem has been solved by the construction of the Ames space eikonometer. This instrument utilizes the characteristic spatial distortions produced by the aniseikonic errors in binocular vision. Using the space eikonometer, Ogle and Madigan⁹ were able to demonstrate that there is, indeed, a relationship between the declination error produced by the oblique astigmatism and the incorrect spatial localization of a binocularly seen vertical line. In the majority of cases a relationship was found between the declination errors computed¹⁵ on the basis of the existing astigmatism and the declination errors measured by the amount of the spatial distortion. The incorrect appearance of objects in space can be corrected by offsetting the measured declination error with meridional magnifying lenses at oblique axes.⁹

It was of importance to investigate to what extent patients would benefit from the correction of the declination errors by equalizing the ocular images. The present paper is a report on the results obtained in a first group of patients for whom were prescribed aniseikonic corrections at oblique axes based on measurements with the space eikonometer.

Before we describe the method of measurement employed and the results obtained, one more point must be discussed.

It still seems to be the general opinion that the incorrect binocular spatial orientation due to the deformation of the retinal image by spectacle lenses, in particular cylindric lenses, while capable of causing ocular discomfort, usually disappears with continued wearing of the lenses, espe-

14 This is not to imply, however, that all aniseikonic errors arise in the correction of refractive anomalies or that the magnitude of the aniseikonia expected on the basis of the refractive error will be measured (Burian, H. M., and Ogle, K. N. A Study of the Aniseikonia in a Case of Increasing Unilateral Index Myopia, *Am J Ophth* **26**:480, 1943).

15 The declination error can be computed on the basis of the astigmatism present if the physical dimensions of the glasses, the eye wire distance and the keratometer readings are known. For details, see Ogle and Madigan⁹.

cially in young people.¹⁶ This opinion, based on ophthalmologic experience, implies that the aniseikonic error which gave rise to the spatial distortion also disappears.

However, aniseikonic errors produced by corrections for anisometropia can often be measured in patients who have worn their glasses for many years and who ordinarily notice no spatial distortions. Nevertheless, the spatial distortions corresponding to aniseikonic errors can be demonstrated under appropriate experimental conditions.¹⁷ The presence of a declination error of the calculated amount in patients who have worn their glasses for as long as fifty years has been found by Ogle and Madigan⁹.

Furthermore, the study of one of us (H. M. B.)¹⁸ on the effect of prolonged wearing of meridional size lenses on spatial orientation certainly suggests that only a small fraction, if any, of the image size differences introduced by the lenses disappears. Whether or not the incorrect spatial localization caused by the aniseikonic error will be manifest depends on the absence or presence of strong perspective clues in the person's surroundings. In the presence of strong perspective clues, such as are contained in the normal surroundings of all city dwellers, the stereoscopic stimuli which would lead to an incorrect binocular spatial localization soon become ineffective.

The fact that a patient is unaware of any spatial distortion is not evidence that aniseikonic errors do not exist. We shall revert to this point once more when discussing the results obtained with patients wearing oblique aniseikonic corrections.

INSTRUMENTS AND PROCEDURE

Instruments.—A meridional aniseikonic error at an oblique axis can be determined if, in addition to the usual measurements of the image size differences in the horizontal and vertical meridians, the vertical declination error can be found. As was pointed out, the Ames space eikonometer¹⁹ makes these measurements possible. In previous papers it has been shown that a good correlation exists between the aniseikonia

16 Hofmann, F. B. *Raumsinn des Auges*, in Graefe, A., and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, ed. 2, Berlin, Julius Springer, 1925, vol. 3, chap. 13, pp. 109-112. More recently, Jackson, E. *Practical Importance of Aniseikoma*, *Am J Ophth* **26**:18, 1943.

17 Ogle, K. N. Association Between Aniseikonia and Anomalous Binocular Space Perception, *Arch Ophth* **30**:54 (July) 1943.

18 Burian, H. M. Influence of Prolonged Wearing of Meridional Size Lenses on Spatial Localization, *Arch Ophth* **30**:645 (Nov) 1943.

19 Ames, A., Jr. The Space-Eikonometer Test for Aniseikonia, *Am J Ophth* **28**:248, 1945.

measured in the horizontal and vertical meridians on the standard eikonometer and that measured on the space eikonometer¹⁷ and, also, that the declination error can be measured on the space eikonometer.⁹ The space eikonometer, therefore, was used to determine the oblique aniseikonic prescriptions given the patients considered in this study.

The Space Eikonometer.—The essential parts of the space eikonometer (fig 2) are (1) a system of selected test elements, (2) suitable test magnifying lens units, by which the size of the images in the two eyes can be changed optically, and (3) a head rest.

The test elements consist of (a) an oblique cross made up of two smooth-stretched cords at right angles to each other and (b) two pairs of smooth vertical plumb cords, erected two in front and two behind the cross.

The oblique cross, stretched from the corners of a 5 foot (152 cm) square frame, is set up vertically at a distance of 3 meters from the subject's eyes. The plane of the cross is carefully erected at right angles to the subject's objective median and visual (horizontal) planes. In the plane of the cross, and through its center, a plumb line is suspended.

Two of the vertical plumb cords are suspended 60 cm in front of, and two 60 cm behind, the cross. The cords in front of the cross are separated about 50 cm, and they thus subtend a visual angle of approximately 12 degrees to the observer. The cords are equidistant from the subject's objective median plane, and the plane of each set of cords is parallel with his frontal plane. Suitable apertures restrict the subject's binocular field of view entirely to the test elements and also prevent him from seeing the ends of the cords. In order to aid in their identification, the cords of the cross are red, the vertical cords in front are green, and the central cord through the cross and the two rear vertical cords are white. The test elements are illuminated by four Lumiline lamps placed so as to produce no shadows. The elements are seen against a uniformly black background.

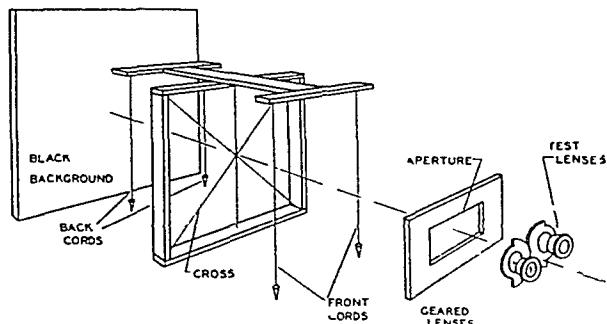


Fig 2.—Perspective drawing of the essential parts of the space eikonometer.

The test magnification lens system (fig 3) consists of two parts. 1. Two pairs of meridional adjustable size units which measure up to 400 per cent,²⁰ one pair before each eye. One pair is fixed at axis 90 (to change the size of the retinal image in the horizontal meridian) and the other at axis 180 (to change the size of the retinal image in the vertical meridian). The magnifications of these lenses then can be adjusted

20 Ogle, K. N. An Optical Unit for Obtaining Variable Magnification in Ophthalmic Use, J. Optic Soc. America 32:143, 1942.

to equalize the horizontal and vertical components of the aniseikonic error in either eye. 2. A matched pair of 200 per cent meridional size lenses, one before each eye, are geared together so that they rotate in equal amounts but in opposite directions. These lenses permit one to offset the vertical declination error caused by a meridional aniseikonic error at an oblique axis by introducing a declination error in the opposite direction without disturbing the horizontal or vertical image size relationships. The two lenses can be rotated, and

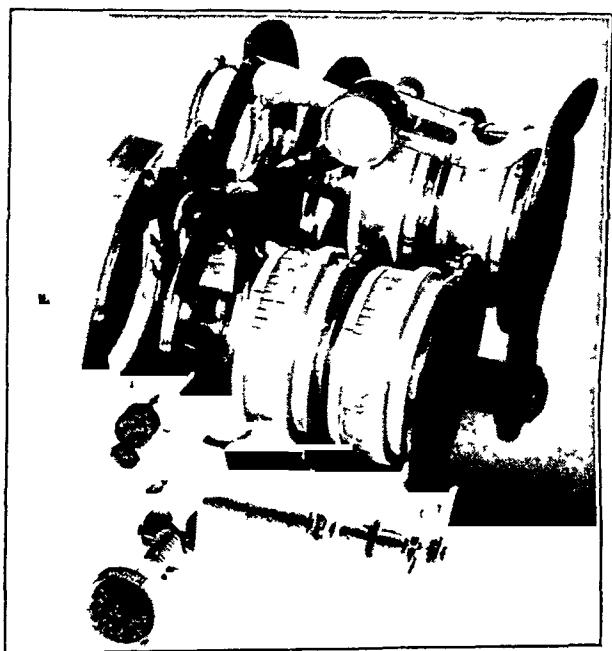


Fig 3.—Photograph of the test lenses on the space eikonometer, showing the adjustable size units for axis 90 and axis 180 measurements, and the geared meridional size lenses by which the declination errors between the two eyes can be measured.

the degree of rotation is indicated on a scale. When the axes of the two lenses are parallel (and vertical), the magnification of one lens offsets the magnification of the other, and their combined binocular effect is zero. If the two lenses are rotated through a small angle, their axes converge upward or downward and introduce, or correct, a vertical declination of the images of the two eyes. The vertical and the horizontal component of the two lenses offset one another. The scale is calibrated to read directly the declination angle (δ) in degrees.²¹

The head rest supports the head and keeps the eyes of the subject properly centered before the instrument.

Procedure.—If a difference exists in the size of the ocular images in the two eyes, or is introduced by size lenses, in the horizontal meridian only, one of each pair of the vertical cords will appear nearer the subject than does the other. Also, the oblique cross will appear rotated about a vertical axis. The nearer cord and the nearer side of the cross will be on the side of the eye having the smaller ocular image. By increasing the size of the image in this eye in the horizontal meridian by means of the appropriate magnifying test

21 The relationship between the vertical declination angle, δ , and the angle of rotation of the geared lenses ρ , is given by the formula $\delta = 0.29 m \sin 2\rho$, in which m is the per cent of magnification of the meridional size lenses (200 per cent in the present instrument).

lens, the cords and the two sides of the cross can be made to appear equidistant from the observer.

If a difference in the size of the ocular images exists, or is introduced by size lenses, only in the vertical meridian, the cross alone will appear rotated about a vertical axis (the vertical cords will be unaffected), the farther side being on the side of the eye having the smaller image. By magnifying the image in that eye in the vertical meridian by means of the appropriate test lens, the two sides of the cross can be made to appear the same distance from the subject, i.e., frontoparallel. Thus, the presence and magnitude of a horizontal and a vertical image size difference can be detected and measured by the difference in the apparent rotation of the vertical plumb lines and the cross. When both a horizontal and a vertical image size difference exist, the horizontal one must be corrected first.

If a meridional image size difference is present at an oblique axis, so that there is a resulting declination error in the ocular images of vertical lines, then the plane of the cross appears inclined (as though rotated about a horizontal axis through the center of the cross).²² If the upper part appears inclined away from the observer, the axes of the correcting meridional size lenses must be rotated so as to converge upward toward the median plane (forehead) of the subject in order to correct that inclination. The measured declination error, δ_m , is said to be positive in this case. If the upper part of the cross appears inclined toward the subject, the axes of the correcting meridional size lenses must be rotated so as to converge downward toward the median plane (chin) of the subject in order to correct that inclination. The measured declination error, δ_m , is said to be negative in this case. By rotating the geared lenses by the proper amount and in the proper direction, the apparent inclination of the plane of the cross can be varied until it and the central vertical cord, through the center of the cross, appear in the same plane. The degree of rotation of the geared lenses measures the vertical declination error.²³ The incorrect apparent orientation of any one of the test elements during the test may affect the relative orientation of the others, so that the final result must be determined in successive approximations by correcting in sequence the horizontal and the vertical image size differences and then by correcting the declination errors.

The data are obtained in the same manner as are the data with the standard eikonometer, namely, by questioning the subject regarding the apparent positions of the test elements as the examiner makes different adjustments of the test lenses. Here, too, the method of limits within which the test elements appear correctly oriented is applied to obtain the final correction. An estimate of the stereoscopic sensitivities of the patient to the three parts of the test is given by one-half

22 Under ordinary circumstances one would expect the cross alone to appear vertical, while the vertical cords should appear inclined, instead of the reverse. Experiment has shown, however, that the apparent angle between the vertical central cord and the apparent position of the plane of the cross is the same in either case (Ogle, K. N. Theory of the Space Eikonometer, to be published).

23 The direction of the calculated correction for the declination error, δ_c , in a given case will be positive if the axes of the correcting minus cylinders converge upward, and it will be negative if they converge downward.

the range within which he reports the vertical cords and the cross to be properly oriented.

The final aniseikonic correction follows directly from the measurements in a straightforward manner. It can be obtained by referring to prepared tables.²⁴ The validity of the correction is usually checked on the space eikonometer, trial magnifying lenses being used.

RESULTS AND COMMENT

Aniseikonic corrections at oblique axes were prescribed for a total of 76 patients. Nearly all these patients had an astigmatic correction of at least 0.50 D cyl in one eye, the axis deviating from the horizontal and the vertical by at least 15 degrees. The ages of the patients ranged from 17 to 70 years, the average age being about 39 years. The patients have worn the aniseikonic corrections at least nine months, the majority have worn them over two years.

On receiving their correction, the patients were asked to report their reactions to the lenses after having worn them for one month and then, again, later. After the study had been in progress for one and a half years, a questionnaire was sent out. A large proportion of the patients have been reexamined since they received their glasses.

In attempting to evaluate the results obtained thus far, one must keep in mind that the patient material in this study was highly selected. The asthenopic symptoms of the patients were, on the whole, much more severe than those of the average patient. Many of the patients had tried, with more or less success, numerous refractive, prismatic and even standard aniseikonic corrections. The oblique aniseikonic correction was tried with several patients only as a last resort. With some of the patients other ocular

24 The tables are based on the following theory. Any given aniseikonic correction consists of an over-all magnification, $o\%$, combined with a meridional magnification $f\%$, at axis ϕ . The formula, then, for the component of that correction in the horizontal meridian (axis 90) is $h = o + f \sin^2 \phi$, and the formula for the component in the vertical meridian (axis 180) is $v = o + f \cos^2 \phi$. The correction for the declination error between the two eyes will be given by the formula $\delta = 0.29 f \sin 2\phi$.

If, as a result of measurement h , v and δ are known, o , f and ϕ can be found. One has for ϕ the formula $\tan \phi = 3.5 \delta / (v-h)$. The meridional per cent of magnification, $f\%$, will be given by the formula $f = [(v-h)^2 + (3.5 \delta)^2]^{1/2}$, or $f = 3.5 \delta / \sin 2\phi = (v-h) / \cos 2\phi$. Then the per cent over-all magnification, $o\%$, will be given by the formula $o = \frac{1}{2} (v + h - f)$.

Under certain conditions the correction can be transformed so that the axes of the meridional corrections will coincide with the axes of astigmatism of the two eyes. In general, this consists of an over-all correction together with a meridional correction for each eye (Ogle, K. N. Meridional Magnifying Lens Systems in the Measurement and Correction of Aniseikonia, J. Optic Soc America 34: 302, 1944).

Tabulation of Data and Results Obtained on Patients to Whom Oblique Anisokonic Prescriptions Were Given

One A.C. No 1r	Chief Complaints	Correction Worn *	Correction Given *	Visual Acuity		Phoria ↓ Near Vision		Percentage Anisokonia ↓ Axis 90		Measured Error Degree		Equivalent Anisokonic Prescription, %	Results
				Distant Vision	Stereop- sensitivity †	Ortho	$\frac{1}{2}\Delta X$	R 1.25	R 0.50	+ 0.20	+ 0.11	R 1.25 x 60	Improvement in head aches
1 10	Frontal headaches	-0.50 -0.25 x 180 -0.25 -0.25 x 60	-0.62 -0.37 x 30 -0.37 -0.25 x 60	20/15 20/15	100	Ortho	$\frac{1}{2}\Delta X$	± 0.25	± 0.60	± 0.10	+ 0.11	R 1.25 x 60	Improvement in head aches
2 12	Severe eyestrain, frontal head aches	+1.25 -1.50 x 30 +1.00 -1.25 x 170	+1.75 -1.50 x 40 +1.50 -1.25 x 170	20/15 20/15	100	$\frac{1}{2}\Delta X$ $\frac{1}{2}\Delta RH$	$\frac{1}{2}\Delta X$ $\frac{1}{2}\Delta RH$	± 0.25	± 0.75	± 0.20	+ 0.54	R 0.50 x 125 L 2.00 x 40	Marked relief
1 33	Ocular discomfort, photopho- bia, nervousness	+0.50 -0.50 x 25 -0.25 -0.37 x 170	+0.75 -0.75 x 25 +0.25 -0.50 x 65	20/20+ 20/20+	100	$\frac{1}{4}\Delta X$	$\frac{1}{4}\Delta X$	± 0.25	± 0.25	± 0.20	+ 0.23	L 1.00 x 120	No benefit
1 30	Ocular fatigue, headaches	-0.87 -0.25 x 45 -0.87 -0.25 x 135	-1.00 -0.25 x 40 -1.00 -0.75 x 115	20/20+ 20/20+	No record	Ortho	Slight X	L 1.00 ± 0.50	L 0.25 ± 0.25	+ 0.29 ± 0.10	+ 0.39	R 0.50 x 60 L 1.25 x 120	Marked relief
5 18	Eyestrain	+1.25 -3.50 x 10 +0.25 -2.62 x 164	+1.00 -3.25 x 10 +0.50 -2.75 x 170	20/20 20/20	100	$0\frac{1}{2}\Delta X$	$2\Delta X$	± 0.37	± 0.50	± 0.20	+ 1.00	R 2.50 x 10 L 1.00 x 90	Marked benefit from correction
6 31	Severe eyestrain and disabling headaches	-0.75 -1.25 x 155 +0.75 -1.00 x 177	-0.75 -1.25 x 155 +0.75 -1.00 x 177	20/40 20/30	90	$2\Delta S$	$2.4\Delta S$	± 0.50	$R 2.00$ ± 1.00	-0.20	- 0.39	R 2.50 x 160	Definite relief from oblique axis correction
7 67	Dysache and headaches, ner- vous tension	+1.00 -5.00 x 100 +1.25 -4.60 x 75	+1.60 -5.60 x 100 +2.00 -5.00 x 73	20/20 20/20	No record	$\frac{1}{2}\Delta S$	$6\Delta X$	± 0.75	$L 1.75$ ± 0.62	-0.85	- 1.45	R 1.25 x 100 L 1.50 x 63	Increased relief with oblique axis correction
8 62	Severe headaches and ocular discomfort	-1.00 -4.00 x 145 +3.50 -1.50 x 125	-0.50 -4.00 x 143 +3.50 -1.50 x 120	20/40# 20/15	100	$2\frac{1}{2}\Delta S$	$5\Delta X$ $1\Delta LH$	$R 4.50$ ± 1.60	-1.12 ± 0.38	- 0.82	R 1.50 O A - 4.50 x 143	Marked comfort from oblique axis correction	
9 18	Marked ocular fatigue, frontal headaches in close work	+0.12 -0.12 x 180 -0.25 sph	Piano Piano	20/15 20/15	100	Ortho	$1\Delta X$	$R 0.75$ ± 0.50	$R 0.50$ ± 0.50	- 0.38	0.00	R 1.50 x 135	Marked relief
10 23	Constant headaches, ocular fa- tigue, inability to read even for few minutes	+0.75 -0.25 x 7 +0.75 -0.25 x 7	+1.50 -0.25 x 45 +1.50 -0.25 x 135	20/15 20/15	100	$\frac{1}{2}\Delta X$	$1\Delta X$	± 0.25	$R 0.50$ ± 0.25	± 0.30	+ 0.28	R 1.50 x 45	Excellent result, patient able to work 10 1/2 hours a day
11 52	Blurring, headaches, associated with use of eyes, photophobia	0.00 -0.37 x 110 0.00 -0.25 x 5	0.00 -0.37 x 20 +0.37 -0.37 x 45	20/15 20/15	100	$1\Delta S$	$2\frac{1}{2}\Delta X$	$R 0.50$ ± 0.25	$R 0.50$ ± 0.25	-0.20	- 0.21	R 0.75 x 120	Partial relief
12 18	Blurring of vision, headaches after reading or movies	+0.75 -0.75 x 75 +0.75 -0.75 x 15	+1.25 sph +0.60 -0.60 x 15	20/15 20/20+	100, slow	Slight S	$2\Delta X$	$R 2.75$ ± 1.00	0.00 ± 1.00	- 0.73	- 1.05	R 3.00 x 105 L 1.00 x 115	Definite benefit
13 11	Severe eyestrain and irritation, photophobia, headaches	+1.00 -3.25 x 168 +1.25 -2.25 x 40	+1.00 -2.75 x 103 +1.00 -2.25 x 40	20/15 20/15	100	$\frac{1}{2}\Delta S$	$5\Delta X$ $2\frac{1}{2}\Delta LH$	$R 0.50$ ± 0.50	$R 2.50$ ± 0.50	-1.30	- 1.70	R 2.25 x 143 L 0.50 x 155	No relief
14 57	Ocular fatigue, photophobia, frontal headaches	+1.00 -5.00 x 72 +1.00 sph	+1.00 -5.00 x 72 R 0.75% x 90 L 1.50% x 180	20/40 20/25	100	$\frac{1}{2}\Delta X$	$4\Delta X$	$R 0.75$ ± 0.25	$L 1.00$ ± 0.25	$+0.55$	+ 0.95	R 2.00 x 72 L 1.50 x 170	Partial relief
15 23	Headaches, eyestrain	+1.25 -1.25 x 15 +1.25 -1.00 x 176	+1.25 -1.25 x 15 +1.25 -1.00 x 176	20/15 20/15	100	Slight X	$1\Delta X$	$R 1.00$ ± 0.25	$R 0.25$ ± 0.37	$+0.29$	+ 0.39	R 1.50 x 60	Definite benefit from oblique axis correction
16 31	Extreme eyestrain, inability to use eyes, nausea, nervousness, distortion of space and form	+0.37 -3.50 x 22 +0.25 -3.50 x 170	+0.37 -3.50 x 15 +0.37 -3.50 x 170	20/20+ 20/20+	100	$2\Delta S$	$6\Delta S$	$L 0.50$ ± 0.50	$+0.96$	$+1.62$	R 1.75 x 46 L 2.00 x 135	Marked relief	

17	13	General ocular distress, inability to wear glasses, headaches	+2 25 -175 177 +1 00 -3 75 149	+2 00 -3 50 180 +1 75 -4 00 150	20/20 20/20	100	Ortho	7Δ X	R 25 ± 0.50	0.00	+ 0.75 ± 0.20	+ 1.32 - 0.20	R 250 OA - 200 150	Symptoms partially relieved, patient able to wear glasses constantly
18	38	Severe headaches, photophobia, difficulty in space perception, nervousness	-5 00 -1 25 19 -5 00 -0 60 167	-1 00 -1 25 180 -2 50 △B 1 -1 00 -0 50 150	20/10+ 20/10+	100	1Δ X	12Δ X	R 185 ± 1.00	R 050 ± 1.00	- 0.46 ± 0.38	+ 0.29 - 0.12	R 300 115 L 076 150	Marked benefit
19	29	Ocular fatigue, headaches, blurring vision, photophobia	-2 75 -0 50 130 -1 25 -0 50 50 R 1 50% A 90	-2 50 -0 75 145 +1 75 -1 00 40	20/16 20/16	No record	5Δ X 1Δ RH	10Δ X	0.00 ± 0.37	L 025 ± 0.60	+ 0.29 ± 0.20	- 0.12 - 0.27	R 050 55 L 076 150	Marked relief, but evidence not convincing
20	18	Eyestrain and headaches	+0 75 -0 75 95 +0 75 -0 37 45	+2 00 -0 75 70 +1 75 -1 00 40	20/16 20/16	100	1Δ S	4Δ X	R 035 ± 0.25	L 075 ± 0.50	- 0.20 ± 0.20	- 0.27 - 0.27	L 100 23 L 100 150	Marked relief
21	16	Ocular irritation, nervousness, photophobia	+2 50 -2 50 180 +2 35 -2 75 10 R 0 75% A 90	+2 50 -2 50 180 +2 00 -2 50 18 L 1 50% A 180	20/20 20/15	100	1Δ X 12Δ LH	8Δ X 12Δ LH	R 025 ± 0.25	R 100 ± 0.37	- 0.38 ± 0.16	- 0.12 - 0.12	R 125 45 R 125 150	No definite relief
22	44	Headaches and nausea when reading, eye discomfort	+1 37 -1 00 32 +1 12 -0 75 2	+1 50 -1 00 40 +1 25 -0 75 180	20/20+ 20/20+	100	4Δ X	7Δ X	R 075 ± 0.25	L 025 ± 0.25	+ 0.29 ± 0.20	+ 0.35 + 0.35	R 150 x10 L 076 180	Much more comfortable with new correction
23	32	Constant headaches, photo- phobia and eyestrain	+1 60 -0 76 65 +1 00 -0 37 160 R 1 00% A 90	+1 50 -0 76 65 +1 25 -0 50 150	20/16 20/16	100	1Δ S	1Δ X	R 075 ± 0.25	R 075 ± 0.50	+ 0.20 ± 0.10	+ 0.35 + 0.35	R 176 OA L 125 150	Partial relief
24	32	General fatigue, occipital and frontal headaches, reading difficulties	+0 50 -0 60 20 +0 75 -0 25 65	+0 75 -0 75 20 +0 75 sph	20/20 20/20	100	4Δ X	4Δ X	R 050 ± 0.25	R 200 ± 0.50	+ 0.29 ± 0.10	+ 0.16 + 0.16	R 150 20 R 150 150	No benefit
25	19	Ocular distress, photophobia, headaches of long standing	+3 50 sph +3 50 sph L 1 00% A 2 2% A 10	+4 25 -0 50 140 +4 50 -0 50 60	20/13 20/13	No record	2Δ X 12Δ LH	2Δ X	L 150 ± 0.25	L 100 ± 0.25	- 0.20 ± 0.16	- 0.32 - 0.32	R 100 145 L 175 OA	Partial relief, more comfort with oblique axis correction than any previous one
26	11	Ocular fatigue, nervous tension	+2 00 -0 25 15 +2 00 -0 37 120	+2 25 -0 50 45 +2 25 -0 60 120	20/20+ 20/16-	90° slow	4Δ S	3Δ X	R 025 ± 0.25	R 025 ± 0.25	+ 0.20 ± 0.10	+ 0.36 + 0.36	R 075 45 R 075 150	Partial relief
27	18	Severe ocular fatigue, vacuity, photophobia	+1 25 -1 00 90 +1 25 -1 62 93	+1 50 -1 25 85 +1 60 -2 00 95	20/16+ 20/16	100	4Δ X	6Δ X	L 025 ± 0.25	0.00 ± 0.25	+ 0.38 ± 0.20	+ 0.24 + 0.24	R 0 50 35 L 100 125	Definite help from glasses
28	43	General ocular distress and irritation, reading difficulty, headaches	+0 25 -0 50 110 +0 25 -0 60 10 L 1 00% A 90	+0 50 -0 50 140 +0 50 -0 50 15	20/16 20/16	100	Slight S	3Δ X 1Δ LH	R 050 ± 0.50	R 50 ± 0.60	- 0.38 ± 0.20	- 0.45 - 0.45	R 100 145 L 130 155	No benefit
29	55	Constant headaches	+1 25 -0 75 122 +1 50 -0 50 75	+2 00 -1 00 120 +2 75 -1 00 60	20/15+ 20/15	100	2Δ X	6Δ X	R 075 ± 0.75	R 025 ± 0.75	- 0.38 ± 0.20	- 0.78 - 0.78	R 125 120 R 125 150	Marked relief from headaches
30	50	Headaches and photophobia	+0 87 -0 37 60 +0 75 -0 37 170	+0 87 -0 37 40 +0 75 -0 25 20	20/16 20/15	100	2Δ S	4Δ X	R 125 ± 0.50	R 25 ± 0.50	+ 0.20 ± 0.20	+ 0.11 + 0.11	R 125 40 L 100 20	Benefit from oblique axis correction
31	33	Eyestrain and eyeache, followed by sick headaches, difficulties in space perception	+1 37 -1 37 39 +1 37 -1 37 148	+2 25 -1 50 30 +2 00 -1 50 150	20/15 20/15	100	1Δ X	5Δ X	R 075 ± 0.25	R 050 ± 0.25	+ 0.38 ± 0.10	+ 0.96 + 0.96	R 125 50 R 125 150	Definite improvement
32	18	Severe and continuous head- aches, fatigue	-0 50 -0 25 85 -0 12 sph	-0 50 -0 50 80 Piano -0 25 135	20/16+ 20/16+	100	Ortho	2Δ X	R 050 ± 0.25	L 025 ± 0.25	+ 0.29 ± 0.16	+ 0.08 + 0.08	R 175 60 L 075 OA - 0 25 130	Partial relief
33	63	Eyestrain, inability to read	-0 62 -1 00 155 -0 50 -2 00 172 5	-0 62 -1 00 155 -0 50 -2 00 172 5	20/15 20/15	100	1Δ S 1Δ RH	4Δ X 1Δ LH	L 125 ± 0.25	L 050 ± 0.37	- 0.80 ± 0.20	- 0.72 - 0.72	R 075 155 L 275 175	Complete relief
34	29	Eyestrain	-0 25 -0 25 60 -0 12 -0 25 116	-0 25 -0 25 45 0 00 -0 50 116	20/15 20/15	100	Slight S	1Δ X	R 050 ± 0.25	R 75 ± 0.25	+ 0.20 ± 0.12	+ 0.30 + 0.30	R 125 345 R 125 150	No benefit
35II	66	Severe eyestrain and frontal headaches of long standing	+5 00 -1 75 60 +4 75 -1 75 115	+5 50 -1 75 60 +5 00 -1 75 120	20/20-2 20/20-3	No record	3Δ S	2Δ X	L 00 ± 0.25	L 150 ± 0.25	+ 0.85 ± 0.20	+ 1.70 + 1.70	R 100 60 L 250 150	Marked relief

Tabulation of Data and Results Obtained on Patients to Whom Oblique Aniseikonic Prescriptions Were Given—Continued

Case No.	Age, Yr	Chief Complaints	Correction Worn*	Correction Given*	Phoria		Aniseikonia		Equivalent Aniseikonic Prescription, %		Results	
					Distant Vision	Near Vision	Measured Δ_m	Calculated Δ_m	Degrees	Degrees		
36	18	Photophobia, ocular discomfort at near work and movies, constant headaches of long standing	+0.50—0.50 ×30	+0.75—0.75 ×80 +0.50—0.25 ×70	20/15 20/15	100 100	1△ X	6△ X	R 0.50 ± 0.25	R 0.50 ± 0.20	+ 0.15 — 0.75	R 0.50 O A — 0.75 A
37	60	Constant frontal and temporal headaches, not associated with use of eyes	+0.25—0.25 ×97	0.00—0.75 ×105 0.00—0.50 ×60	20/15 20/15	100 100	1△ S	9△ X	L 0.50 ± 0.50	L 0.50 ± 0.50	— 0.38 — 0.30	L 1.00 ×60 No relief from head aches
38	33	Headaches, especially on dry int., infrequent headaches rendering difficulties	Plano—0.75 ×60 Plano—1.50 ×155	Plano—0.75 ×60 Plano—1.50 ×155	20/15— 20/15—	100 100	2△ X	2△ X	R 1.25 ± 0.25	L 0.50 ± 0.50	+ 0.50 — 0.55	R 2.00 ×60 L 1.00 ×155 Marked relief
39	31	Severe headaches, eyestrain, fatigue, some headaches	+0.25—0.25 ×90 +0.50—1.75 ×25	+0.25—0.25 ×90 +0.50—1.75 ×25	20/20— 20/20—	100, slow	1½△ X 1½△ RH	5½△ RH	R 0.75 ± 0.25	L 1.50 ± 0.50	— 0.53 — 0.20	L 1.25 ×25 Improvement in head aches
40	32	Need for glasses, ocular fatigue, some headaches	None	+0.62 sph +2.50—1.75 ×55	20/15+ 20/20—	100 100	1△ S	Ortho	R 2.25 ± 0.20	R 2.50 ± 0.60	— 0.55 — 0.20	R 1.00 O A — 2.00 ×135 Very satisfactory
41	52	Headaches and ocular pain, ocular fatigue and nervousness, difficulties in space perception	+1.50—1.37 ×170 +1.50—1.37 ×55	+1.50—1.50 ×165 +1.75—1.50 ×55	20/15 20/15	100 100	1△ X	7△ X	R 0.50 ± 0.25	R 1.25 ± 0.25	— 0.38 — 0.30	R 1.75 ×155 No help from glasses
300	39	H headaches, reading difficulty	+2.50—4.00 ×165 —1.75—0.75 ×180	+2.50—4.00 ×165 —1.75—0.75 ×180	20/20 20/15	100 100	1½△ S	6△ X	L 0.50 ± 0.75	L 0.25 ± 0.25	— 0.38 — 0.60	L 1.50 ×46 Possibly some benefit
43	33	Headaches and eyestrain, ocular fatigue	+1.50—1.25 ×180 +0.75—1.00 ×30	+2.25—1.25 ×180 +1.25—1.00 ×30	20/15 20/20	70 70	Ortho	1½△ S	R 0.75 ± 0.25	0.00 ± 0.25	— 0.20 — 0.10	R 0.75 O A L 0.75 ×120 Partial relief
44	30	Eyeache, frontal and occipital headaches on use of eyes, of long standing, photophobia	+2.75—3.25 ×20 +3.25—4.00 ×140	+2.50—3.50 ×20 +3.25—4.00 ×140	20/15 20/15	100 100	1½△ S 1½△ LH	4½△ X 1½△ RH	R 1.00 ± 0.25	R 0.25 ± 0.25	+ 1.00 ± 0.20	R 3.00 ×50 L 1.00 ×140 Marked relief
45	41	Frequent headaches, nervousness	+1.12—0.37 ×10 +1.00—0.50 ×45	+1.25—0.37 ×90 +1.37—0.87 ×60	20/20 20/20	No record	Ortho	1△ X	0.00 ± 0.50	L 0.25 ± 0.37	— 0.29 — 0.12	— 0.37 — 0.12
46	30	Ocular fatigue, especially for near work, nervousness	+1.75—0.62 ×15 0.50% O A	+1.75—0.62 ×115 +2.00—0.87 ×165	20/15—2 20/20+2	No record	1△ S	2△ X	L 0.75 ± 0.20	L 0.25 ± 0.25	+ 0.16 + 0.18	L 1.00 ×15 Definite relief with oblique axis correction
47	11	General ocular discomfort and fatigue, poor reader	+1.12—3.50 ×3 +0.75—1.00 ×90	+1.10—3.50 ×5 R 2.00% ×180	20/20 20/20	100 100	1△ X	6△ X	R 3.00 ± 0.50	0.00 ± 0.50	+ 0.38 — 0.15	R 3.00 O A L 3.00 ×167 Former aniseikonic correction gave unusual relief but oblique axis correction much better
48	40	Frontal headaches, inability to read comfortably	-1.00 sph R 1.50% ×90	-1.00 sph -1.00—0.25 ×20	20/15 20/15	No record	3.3△ X	5.6△ X	R 1.25 ± 0.25	0.00 ± 0.50	+ 0.20 ± 0.10	L 0.75 ×60 Definite benefit
49	23	Constant ocular discomfort, frontal headaches photo phobia, space difficulties	-1.25—3.50 ×170 -1.00—4.00 ×17 -1.00—4.00 ×17 -1.00—4.00 ×17	-1.25—3.50 ×170 -1.00—4.00 ×17 -1.00—4.00 ×17 -1.00—4.00 ×17	20/30+ 20/30+ 20/30+ 20/30+	90, with diff 1△ base up 1△ base down	1△ S 1½△ LH	2½△ X 1½△ LH	L 0.50 ± 0.25	0.00 ± 0.25	— 1.07 — 0.40	R 1.50 ×135 L 1.50 ×45 Considerable benefit from oblique axis correction

·0	26	Headaches and ocular discomfort, photophobia	Phano -0.75 X165 -0.50 -1.25 X10 R 1.00% O A L 0.75% A180	-0.25 -0.75 X160 -0.75 -1.25 X10 +2.25 -1.25 X8 R 2.00% A90	20/15 20/15	70	Ortho	3Δ X $\frac{1}{2}\Delta LH$	R 3.00 ±0.25	R 2.50 ±0.25	L 0.50 ±0.26	-0.20 ±0.12	-0.33	R 1.62 X165 L 1.75 X10	Some benefit from oblique axis correction
51	73	Dystain, continuous head aches, reading difficulties	+1.37 -0.03 X163 +2.00 -0.50 X15 +3.00 -0.50 X160 R 2.00% A90	+2.00 -0.50 X15 +3.00 -0.50 X160 +1.25 sph +5.00 -5.00 X27 5	20/20 20/20	100	Ortho	4Δ X 3½Δ X	R 4.50 ±0.25	R 0.50 ±0.37	R 0.90 ±0.12	-0.95	+0.34	R 1.00 O A -3.25 X60	Very marked relief of symptoms
52	38	Ocular fatigue, effort to read, carshiness	+0.62 -0.37 X98 +3.50 -3.50 X15 -0.25 sph +0.25 -1.00 X37	+1.25 sph +5.00 -5.00 X27 5 0.00 -0.12 X135* +0.25 -1.00 X37	20/13 20/25	100	Ortho	8Δ X 4½Δ X	0.00 ±0.25	L 0.87 ±0.25	-0.55 ±0.10	-0.60	R 0.75 X135 L 1.60 X37	Marked improvement with glasses	
53	41	Headaches, photophobia, eye strain	+1.25 -1.00 X150 +1.25 -1.25 X60 +1.50 -1.25 X63	+1.50 -1.00 X140 +1.50 -1.25 X63 +5.00 -3.00 X15 +3.00 -1.75 X157	20/15 20/15	100	Ortho	8Δ X 4½Δ X	R 0.50 ±0.75	R 0.50 ±0.50	-0.30 ±0.10	-0.67	R 1.00 X110 L 0.75 X63	Patient completely satisfied, relief	
54	46	Headaches from driving and movies, reading difficulties, cannot wear glasses	+1.00 -2.50 X10 +1.75 -1.25 X25 +1.75 -1.25 X157	+5.00 -3.00 X15 +3.00 -1.75 X165 +1.25 -0.50 X170 +3.25 -5.00 X25	20/20 20/20	100	Ortho	2Δ S 2Δ X	L 1.75 ±0.25	L 0.75 ±0.25	+0.38 ±0.20	+0.74	L 1.75 X120	Complete relief	
55	45	Continuous ocular fatigue, space difficulties, vertigo, some headaches	+1.00 -2.50 X10 +1.75 -1.25 X25 +1.75 -1.25 X157	+5.00 -3.00 X15 +3.00 -1.75 X165 +1.25 -0.50 X170 +3.25 -5.00 X25	20/20 20/20	100	Ortho	2Δ S 2Δ X	L 1.75 ±0.25	L 0.75 ±0.50	-1.00 ±0.30	-1.59	R 2.75 O A -0.75 X170 L 4.00 X25	Definite benefit, patient able to read with correction	
56	22	Patient cannot wear glasses for even few minutes, severe eyestrain and headaches	+0.50 sph +1.00 -1.00 X27	+0.50 sph +1.00 -1.00 X27	20/15 20/30	80	Ortho	4½Δ X 2Δ RH	R 2.55 ±0.75	L 0.75 ±0.50	-1.12 ±0.30	-1.81	R 4.00 O A L 4.00 X42	No benefit	
57	18	Eyestrain and discomfort of long standing	+0.50 -0.75 X180 +4.00 -4.00 X43	+1.00 -1.00 X180 +5.00 -5.00 X42	20/20 20/20	80	Ortho	6Δ X 4Δ X	R 2.00 ±0.75	R 2.00 ±0.75	-1.29 ±0.29	-1.81	R 4.00 O A L 4.00 X42	No benefit	
58	62	Ocular fatigue	+6.00 -0.50 X10 +6.50 -2.25 X60	+6.00 -0.50 X10 +6.50 -2.25 X60	20/25 20/20	80	Ortho	18Δ X E cycle 4°	R 1.25 ±0.25	R 0.75 ±0.25	+0.56 ±0.38	-0.58	R 2.50 O A L 2.50 X150	Good results	
59	33	Spatial difficulties, photo phobia	+1.62 -1.12 X170 +1.75 -1.25 X10	+2.25 -1.50 X10 +2.25 -1.50 X170	20/20 20/20	100	Ortho	3Δ X 3Δ LH	R 0.25 ±0.25	L 0.25 ±0.25	+0.38 ±0.12	+0.47	R 2.00 X10 L 2.00 X170	Definite benefit	
60	18	Ocular fatigue, frontal head aches, no help from wearing of correction, carshiness	+0.50 -0.50 X180 +2.25 -3.25 X17	+0.50 -0.50 X175 +2.25 -3.25 X17	20/20 20/20	50,	Ortho	12Δ X slow	R 1.00 ±1.00	R 1.00 ±1.00	-0.55 ±0.38	-1.13	R 2.00 X175 L 3.00 X23	Definite relief, new correction worn constantly	
61	35	Stek headaches, ocular fatigue, space distortion	+1.50 -1.75 X150 +1.00 -1.00 X25 L 1.00% O A	+1.50 -2.00 X155 +0.75 -1.00 X20	20/15 20/15	100	Ortho	2Δ X 2Δ X	L 0.50 ±0.50	L 0.25 ±0.25	-0.38 ±0.20	-1.00	R 0.75 X110 L 1.60 X60	Marked relief	
62	36	Carsickness, air sickness	0.00 -0.25 X165 1Δ BI -0.25 -0.25 X165	+0.50 -0.50 X145 +0.25 -0.25 X45	20/15 20/15	100	Ortho	4Δ X 5Δ RH	R 0.50 ±0.25	R 0.50 ±0.25	-0.20 ±0.10	-0.19	R 0.75 X127	Results indeterminate	
63	55	Ocular discomfort with use of eyes	+1.87 -0.25 X165 +1.87 -0.25 X30	+2.50 -0.25 X135 +2.50 -0.25 X45	20/15 20/15	100	Ortho	5Δ X 5Δ RH	R 0.50 ±0.25	R 0.50 ±0.25	-0.20 ±0.10	-0.10	R 0.50 O A L 1.25 X45	Results uncertain	

* In this column, and in other columns, O A indicates an overall magnification

† Obtained on Keystone DB° chart

‡ X indicates exophoria, S, esophoria, L H, left hyperphoria, R H, right hyperphoria.

§ Aniseikonic measurements made while patient was wearing refractive prescription in standard Tillyer spectacle lenses

|| Probably inaccurate because of oblique prisms in prescription

Corneal scar

** Determined by the proximation method on the standard elkomometer

†† Exophoria prior to operation

factors, such as convergence insufficiency, complicated the problem. Other patients were definitely neurotic. Circumstances compelled us to conduct our study on such a group of patients. Favorable results are, therefore, all the more significant.

We have refrained from a detailed statistical study and have divided the patients roughly into three groups: (1) patients who had definitely been relieved of their symptoms, (2) patients who were partially relieved of their symptoms, and (3) patients for whom the prescription resulted in failure. The data on 13 of the 76 patients had to be discarded because of insufficient information about the result (4 patients) or because definite or probable extraneous factors interfered with the evaluation (5 and 4 patients respectively).

Of the remaining 63 patients, 36 have reported marked relief from their symptoms, 16, partial relief, and 11, no relief whatever. The accompanying table lists the most pertinent data for each of the 63 patients.

We shall now discuss in some detail the results obtained and report the history in representative cases.

REPORT OF CASES²⁵

CASE 1—I. E. B., a woman aged 28, a school teacher, came for examination because of severe "eye-ache," photophobia and frontal and occipital headaches on use of her eyes, especially at moving pictures, in driving and in close work. These symptoms had existed since early in life but had become increasingly severe in the past eight years. She had worn glasses constantly since the age of 12 years. Frequent medical examinations had revealed nothing abnormal. She had been under expert ophthalmic care and was operated on in 1934 and 1935 for exophoria and right hyperphoria, which were discovered by an occlusion test.

Refraction and Visual Acuity—Visual acuity of 20/15 was obtained with a correction of +2.75 D sph —3.25 D cyl, axis 20 for the right eye and of +3.25 D sph —4.00 D cyl, axis 140 for the left eye. At 20 feet (6 meters) there were 1 prism diopter of esophoria and $\frac{1}{2}$ prism diopter of left hyperphoria, at 16 inches (40.6 cm), 4 prism diopters of exophoria and $\frac{1}{2}$ prism diopter of left hyperphoria. Examination for stereopsis revealed 100 per cent depth perception with the Keystone DB 6 chart.

25 Unless it is specifically mentioned, the eyes of these patients had clear media and no pathologic condition of the fundi. Here, δ_m designates the measured declination error, and δ_c , the declination error computed on the basis of the existing astigmatism; the values are recorded in degrees. An estimate of the stereoscopic sensitivity of the patients is given by one-half the range within which the patient reported that the vertical cords and the cross of the space eikonometer were properly oriented. Sensitivities of ± 0.25 per cent for axis 90 and axis 180 and of 0.10 to 0.20 degree for the declination error are considered normal. Aniseikonic measurements and corrections are indicated by the magnification necessary to equalize the ocular images.

Measurements on Space Eikonometer—The measurements for aniseikonia were as follows:

At axis 90, (right) $100\% \pm 0.25\%$

At axis 180 (right) $0.25\% \pm 0.25\%$

Measured declination error, $\delta_m + 100^\circ \pm 0.20^\circ$

Computed declination error, $\delta_c + 2.80^\circ$

The following correction was prescribed:

Right eye +2.50 D sph —3.50 D cyl, axis 20 $\pm 3.00\%$ meridional magnification, axis 50

Left eye +3.25 D sph —4.00 D cyl, axis 140 $\pm 1.00\%$ meridional magnification, axis 140

These glasses were worn as fit-overs for six months, they proved completely satisfactory. Reexamination before the correction was prescribed in permanent form yielded essentially the same measurements. The patient has now worn the permanent glasses for fifteen months and reports great relief from her symptoms except for occasional headaches, which are less severe than in the past.

This case is a typical one in which the high oblique astigmatic correction required by the patient produced a declination error which was of significant amount and in the direction expected from the astigmatic error. The patient showed a high stereoscopic sensitivity, and the correction of the aniseikonia afforded her relief from severe symptoms, of long standing.

This case does not seem to offer particular difficulties in interpretation. There are, however, cases in which the measured and the computed declination errors do not agree. Nevertheless, in some instances the patients are benefited, if the measured declination error is used as the basis for the aniseikonic prescription.

CASE 2—Mrs. R. H. B., a housewife aged 41, engaged in sculpturing and literary work, came for examination because of severe eyestrain, particularly in the right eye, caused by the use of the eyes for distant, as well as near, vision. If close work was continued, frontal headache developed. In bright light and sunshine, as well as in close work, the right eye tended to close. At the age of 8 years the patient had been struck in the right eye by an air rifle bullet. She had worn glasses since attending high school and had always had expert ophthalmic care. The last prescription was given her two years prior to examination at the Dartmouth Eye Institute.

The right eye showed an iridodialysis between 7 and 8 o'clock, and the pupil of that eye was accordingly distorted. Otherwise, both eyes were normal in all parts.

Refraction and Visual Acuity—Visual acuity of 20/15 was obtained with a correction of +1.75 D sph —1.50 D cyl, axis 40 for the right eye and of +1.50 D sph —1.25 D cyl, axis 170 for the left eye. This refractive correction was identical with the one the patient was wearing except for an increase of +0.50 D sphere for each eye. Readings at 20 feet (6 meters) showed 1 prism diopter of exophoria and $\frac{1}{2}$ prism diopter of right hyperphoria, and at 16 inches (40.6 cm), 4 prism diopters of exophoria and $\frac{1}{2}$ prism diopter of right hyperphoria. Examination for stereopsis revealed 100 per cent depth perception with the graduated Keystone DB 6 chart.

Measurements on Space Eikonometer—The measurements for aniseikonia were as follows

At axis 90 (left) $0.25\% \pm 0.25\%$
 At axis 180 (left) $0.75\% \pm 0.25\%$
 Measured declination error (δ_m) — $0.55^\circ \pm 0.20^\circ$
 Computed declination error (δ_c) + 0.55°

The equivalent aniseikonic correction was prescribed as follows

Right eye + 1.75 D sph \square — 1.50 D cyl, axis 40
 \square 50% meridional magnification, axis 125
 Left eye + 1.50 D sph \square — 1.25 D cyl, axis 170 \square
 200% meridional magnification, axis 40

The patient wore these glasses with fit-over size lenses for four months, with good results, and was then given permanent glasses after reexamination, which substantiated the findings of the first examination. When she reported again, two years and four months later, she stated that she no longer had eyestrain or headaches and that her right eye closed only occasionally in bright light. She volunteered the information that objects stood out in relief much better, trees, for instance, were no longer flat on the hill. Her only complaint was that of blurring in near vision for the past year. The measurements revealed no need for a change in the correction for distance, an addition of + 0.75 D sph for each eye was given for reading.

The salient feature of this case is the fact that a declination error was measured in the direction opposite that which would be theoretically expected. According to the patient's astigmatic correction (axes of minus cylinders converging upward), she should have had a declination error which would be corrected by meridional size lenses with axes converging upward (positive declination error). Actually, a negative declination error was measured. Nevertheless, excellent subjective results were obtained by correcting the measured declination error.

It is difficult to explain the discrepancy between the measured and the calculated declination error in this case. Ogle and Madigan⁹ have suggested that a declination error measured in the direction opposite that expected from the astigmatism may be due either to the presence of a cyclotropia or to a basic meridional aniseikonic error, not optical in nature, which is in a direction opposite that introduced by the astigmatic correction.

While at present one can only suggest a possible explanation of the measurements obtained in this case, there are other cases which indicate the direction which future research must take in order to solve this problem. These are the cases (1) in which there is a measurable and clinically significant declination error, in spite of the fact that the patient has a spherical refractive correction or is emmetropic, and (2) in which there is a large amount of oblique astigmatic error, yet no declination error can be measured.

CASE 3—E J I, a Catholic priest aged 40, complained of frontal headaches and "confusion" after reading for fifteen minutes and after driving a car for about one hour, and of inability to concentrate on his reading matter. The trouble began sixteen years ago, after a "nervous breakdown." He was given glasses five years prior to the first examination at the Dartmouth Eye Institute (correction of — 0.75 D sph for each eye).

Refraction and Visual Acuity—Visual acuity of 20/15 in each eye was obtained with the following correction:

Right eye — 1.00 D sph
 Left eye — 1.00 D sph \square — 0.25 D cyl, axis 20

At 20 feet (6 meters) there was 2 to 3 prism diopters of exophoria, and at 16 inches (40.6 cm) 5 to 6 prism diopters of exophoria.

Examination with the standard eikonometer showed that a correction of 150% meridional magnification, axis 90 should be combined with the refractive correction for the right eye. The patient wore this correction for one year and reported that vision was improved with these glasses, but that there were apparent tipping of the floor and distortion of objects. Reexamination showed that the refractive error was unchanged.

Measurements on Space Eikonometer—The measurements for aniseikonia were as follows:

At axis 90 (right) $1.25\% \pm 0.25\%$
 At axis 180 $0.00\% \pm 0.50\%$
 Measured declination error (δ_m) + $0.20^\circ \pm 0.10^\circ$
 Computed declination error (δ_c) 0

The equivalent aniseikonic correction prescribed was as follows:

Right eye — 1.00 D sph \square 150% meridional magnification, axis 105
 Left eye — 1.0 D sph \square — 0.25 D cyl, axis 25

After wearing this correction for four months, the patient reported decided improvement; he was able to do several hours of concentrated reading, without the "confusion" formerly experienced; there were still headaches, but they were much fewer and less severe. After one year the improvement was still present.

In this case a declination error was measured in spite of isometric refraction (except for insignificant astigmatism in the left eye). The results of examination with the standard eikonometer approximated the measurements with the space eikonometer. But the result obtained was much better when the axis of the meridional magnification was rotated by 15 degrees, so that a correction of the measured declination error was effected.

Even more striking is a case in which a declination error was measured in the presence of emmetropia.

CASE 4—S B W, a girl aged 15 years, was a high school student when she was first seen, in 1938. For the past three years she had had severe ocular fatigue and frontal headaches when doing close work, watching moving pictures or riding in a car. Glasses prescribed eighteen months prior to examination here (right eye + 0.12 D sph \square — 0.12 D cyl, axis 180, left eye + 0.25 D sph \square — 0.25 D cyl, axis 5) had not given relief.

Refraction and Visual Acuity—The right eye was emmetropic, with visual acuity of 20/15, the left eye had visual acuity of 20/15 with correction of —0.25 D sph.

At 20 feet (6 meters) there was orthophoria, at 16 inches (40.6 cm), 1 prism diopter of exophoria.

Measurement with the standard eikonometer revealed the need for 100 per cent over-all magnification of the right ocular image. The following correction was given:

Right eye plano lens $\supseteq 100\%$ over-all magnification

Left eye plano lens

The patient returned three years later, stating that the glasses had been of help for about two years but that now, again, she had had frequent frontal headaches. The results of refraction were as follows:

Right eye —0.25 D cyl, axis 150, vision 20/15

Left eye —0.25 D cyl, axis 40, vision 20/15

Examination on Space Eikonometer (performed without refractive correction)—The measurements for aniseikonia were as follows:

At axis 90 (right) $0.75\% \pm 0.50\%$

At axis 180 (right) $0.50\% \pm 0.50\%$

Measured declination error (δ_m) $+0.38^\circ \pm 0.20^\circ$

Computed declination error (δ_c) 0

The following equivalent aniseikonic correction was prescribed:

Right eye plano lens $\supseteq 150\%$ meridional magnification, axis 135

Left eye plano lens

The patient wore this correction with great comfort. Two years and three months later she came for reexamination, at her father's wish, because she had lately experienced eyestrain at the end of the day; she is now engaged in exacting war work.

Measurement on Space Eikonometer—With the patient's correction, the measurements for aniseikonia were as follows:

At axis 90 (right) $1.00\% \pm 0.50\%$

At axis 180 $0.00 \pm 0.50\%$

Measured declination error (δ_m) $-0.20^\circ \pm 0.20^\circ$

Without glasses the measurements for aniseikonia were as follows:

At axis 90 (right) $1.00\% \pm 0.50\%$

At axis 180 (right) $0.75\% \pm 0.62\%$

Measured declination error (δ_m) $0.38^\circ \pm 0.20^\circ$

These measurements indicated that the declination error was somewhat undercorrected, and the following equivalent aniseikonic correction was suggested: right eye, plano lens $\supseteq 175\%$ meridional magnification, axis 130, left eye, plano lens. The patient did not feel that her symptoms warranted a change of glasses at this time.

If there are cases of isometropia or emmetropia with measurable declination errors in which symptoms are relieved when the declination error is corrected, it is logical to assume that there must be cases of astigmatic corrections at oblique axes in which no declination error is shown. Such cases do indeed exist, and the following case is an example.

CASE 5—G. S. J., a woman aged 24, engaged in housework, came to the Dartmouth Eye Institute in 1937. She gave a history of "sick headaches" in her family, and she herself complained of severe frontal and temporal headaches, beginning on the left side and

spreading to the right. The headaches might come at any time and last for days, and they were often completely disabling. Lately they had been accompanied with nausea and vomiting. The vomiting did not relieve the headaches. They were not necessarily connected with the use of the eyes, but her eyes had always been bad. She was subject to eyestrain, and vision was not good. She had worn glasses constantly since the age of 5 years. Because of her headaches and ocular discomfort, she had to give up school when she was a freshman in high school. She had always been under expert medical and ophthalmic care. The removal of wisdom teeth, treatment of sinuses and treatment for migraine headaches were of no avail. The last refractive correction was given nine months prior to the first examination at the Dartmouth Eye Institute.

Refraction and Visual Acuity—The results of refraction were as follows:

Right eye $+3.00$ D sph $\supseteq -4.00$ D cyl, axis 25, vision 20/30

Left eye $+2.50$ D sph $\supseteq -4.00$ D cyl, axis 155, vision 20/30

Findings at 20 feet (6 meters) varied from orthophoria to $\frac{1}{2}$ prism diopter of esophoria, at 16 inches there was 1 to 2 prism diopters of exophoria. Examination for stereopsis revealed 100 per cent depth perception with the graduated Keystone DB6 chart.

Examination on the standard eikonometer indicated the need for over-all magnification by 150 per cent of the ocular image of the left eye. This was incorporated with the refractive correction. The glasses did not help, neither did various refractive corrections or monocular occlusion. The patient was followed for five years, during this time numerous medical examinations, including encephalographic studies, were made, but she obtained no relief.

In January 1942 she was first examined with the space eikonometer. She proved on the whole to be a good observer, though the data showed some variability. Average data obtained in examinations with the space eikonometer over a period of days were as follows:

At axis 90 (left) $0.75\% \pm 0.50\%$

At axis 180 (left) $1.25\% \pm 0.62\%$

Measured declination error (δ_m) $+0.20^\circ \pm 0.30^\circ$

Computed declination error (δ_c) $+1.45^\circ$

Various aniseikonic corrections, on the basis of measurement and of calculation, were tried, but none afforded any relief. Six months later the refractive correction was changed somewhat (right eye, $+3.00$ D sph $\supseteq -4.50$ D cyl, axis 22, left eye, $+2.00$ D sph $\supseteq -4.50$ D cyl, axis 157) and the measurements in the space eikonometer showed improvement in sensitivity. They were as follows:

At axis 90 (right) $0.75\% \pm 0.25\%$

At axis 180 (left) $0.50\% \pm 0.25\%$

Measured declination error (δ_m) $0.00 \pm 0.20^\circ$

Computed declination error (δ_c) 1.45°

The patient wore the refractive correction only, and six months later the aniseikonic data were:

Axis 90 (right) $1.25\% \pm 0.25\%$

Axis 180 (left) $1.75\% \pm 0.25\%$

Measured declination error (δ_m) $0.00 \pm 0.10^\circ$

The aniseikonic error at axes 90 and 180 was prescribed for, but the correction did not afford the patient any relief, and she soon discarded the heavy fit-over glasses.

This case cannot properly be called one of oblique meridional aniseikonia. It is cited because no declination error could be measured in spite of a large oblique astigmatic correction. Nor would it be correct to classify this case as one of failure to correct the oblique meridional aniseikonia. The seat of the patient's difficulty must be sought elsewhere.

There are, however, cases in which the prescription resulted in complete failure, although at least partial improvement might have been expected in view of the large oblique astigmatic error and the close agreement between the measured and the computed data. An illustration is the following case:

CASE 6—F. A. Q., a dentist aged 41, complained of considerable eyestrain (soreness, pulling and smarting of the eyes) after close work, reading, driving and watching motion pictures. There were also photophobia and some headache. The headaches had decreased after a radical antrotomy was performed four years before. The patient had worn glasses constantly since the age of 17 years. The eyestrain had been increasing for the past twelve years. He had always been under competent ophthalmic care, he had had refractive corrections, with and without vertical prisms, for left hyperphoria, monocular occlusion, additional correction for near work, and examination for aniseikonia before coming to the Dartmouth Eye Institute. The aniseikonic glasses with corrections at axes 90 and 180 proved of no help; they were, in fact, less comfortable than the simple refractive correction.

Refraction and Visual Acuity—The results of refraction were as follows:

Right eye +100 D sph ⊖—275 D cyl, axis 163, vision 20/15

Left eye +100 D sph ⊖—225 D cyl, axis 40, vision 20/15

At 20 feet (6 meters) there were 1 prism diopter of esophoria and 3 prism diopters of left hyperphoria, and at 16 inches (40.6 cm), 4 to 6 prism diopters of exophoria and 2½ prism diopters of left hyperphoria. Examination for stereopsis revealed 100 per cent depth perception with the graduated Keystone DB6 chart.

Measurement with the standard eikonometer indicated the need for 200 per cent meridional magnification, axis 180 for the right eye. The following prescription was ordered:

Right eye +100 D sph ⊖—275 D cyl, axis 163 ⊖ 1Δ base up ⊖ 200% meridional magnification, axis 180

Left eye +100 D sph ⊖—225 D cyl, axis 40 ⊖ 2Δ base down

An additional correction of +100 D sph for near work was given for both eyes. This correction did not afford relief, and eight months later measurements were made on the space eikonometer. The findings were as follows:

At axis 90 (right) 0.50% ± 0.50%

At axis 180 (right) 2.50% ± 0.50%

Measured declination error (δ_m) — 1.30° ± 0.20°

Computed declination error (δ_c) — 1.70°

An equivalent aniseikonic correction was suggested, with the addition to the patient's refractive correction of 250% meridional magnification, axis 135 for the

right eye. Examination seven and, again, sixteen months later revealed that the measured declination error was somewhat smaller, but still highly significant. The final equivalent aniseikonic correction arrived at was as follows:

Right eye +100 D sph ⊖—275 D cyl, axis 163 ⊖ 225% meridional magnification, axis 143

Left eye +100 D sph ⊖—225 D cyl, axis 40 ⊖ 0.50% meridional magnification, axis 53

An additional correction of +100 D sph for near vision was given for each eye. This correction was no more satisfactory than were the previous ones, and the patient has since reported that he gets along best with an old refractive correction having neither prismatic nor aniseikonic elements.

It has been pointed out before that as a rule patients with meridional aniseikonic errors at oblique axes are not aware of difficulties in spatial orientation. Occasionally, however, such difficulties are reported. The following case is one in point:

CASE 7—R. A. B., a man aged 24, assistant to a civil engineer, reported that he had worn glasses since childhood but that he had never seen well even with them. He complained of daily frontal and temporal headaches, burning, smarting and watering of the eyes, occasional vertical diplopia, and inability to read for more than half an hour. These difficulties prevented the intelligent young man from going to college. He also reported difficulties in judging distances; he was never good at sports which involved watching a ball and had never driven a car with confidence.

The patient was wearing a correction of —100 D sph ⊖—250 D cyl, axis 160 for the right eye and of —100 D sph ⊖—350 D cyl, axis 30 for the left eye.

Refraction and Visual Acuity—The results of refraction were as follows:

Right eye —125 D sph ⊖—350 D cyl, axis 170, vision 20/25+

Left eye —100 D sph ⊖—400 D cyl, axis 17, vision 20/30+

In view of the significant change, this refractive correction was prescribed. It helped the patient only so far as it gave him better visual acuity, but his symptoms persisted. One year later he returned for another examination. The results of refraction were unchanged. For distance (20 feet) with his correction there were 1 prism diopter of esophoria and 1 prism diopter of left hyperphoria. The left hyperphoria increased to 3 prism diopters in the right half of the field of fixation, an observation which aroused the suspicion that it was based on weakness of the left superior oblique muscle. This suspicion was strengthened by the patient's habit of tilting his head to the right shoulder and the presence, with the Volkmann disk, of a declination of 5.5 degrees in the left eye (as opposed to a declination of 1.6 degrees in the right eye). In stereoscopic examinations the patient could obtain, with difficulty, a score of 90 per cent on the graduated Keystone DB6 chart. The hyperphoria was thought to be a disturbing factor, and the patient was given, in addition to his refractive correction, prismatic fit-over lenses ¾ prism diopter base up for the right eye and 1¼ prism diopters base down for the left eye. He was asked to wear these glasses for two months. On his return he reported that he had great

difficulty with these glasses and that they had had no beneficial effect on his symptoms. In addition to the trouble in judging distances, he now noticed spatial distortions. The floor appeared to rise toward him, and in motion picture theaters the projection screen appeared tipped toward him.

Space Eikonometer Readings—Measurements for aniseikonia were as follows:

At axis 90 (left) $0.50 \pm 0.25\%$

At axis 180 $0.00 \pm 0.25\%$

The measured declination error, δ_m , varied within wide limits, from -1.38 to -1.10 degrees, and the patient had a low stereoscopic sensitivity. After several days of testing, the declination error became more certain and was estimated to be about -1.00 degree. The computed declination error, δ_c , was -1.50 degrees. Accordingly, the following equivalent aniseikonic correction was prescribed:

Right eye 1.50% meridional magnification, axis 135
Left eye 1.50% meridional magnification, axis 45

This correction was given the patient as fit-over size lenses to be worn with his refractive correction, incorporating prisms.

After the patient had worn these glasses two months, he returned for examination. Measurements on the space eikonometer with his aniseikonic fit-over lenses were as follows:

At axis 90 (left) $0.25\% \pm 0.25\%$

At axis 180 $0.00 \pm 0.50\%$

Measured declination error, δ_m $0.00 \pm 0.40^\circ$

Without the fit-over lenses the measured declination error, δ_m , was $-1.07^\circ \pm 0.38^\circ$. He reported that his symptoms were much improved, and he had done much more close work than in the past. Although he still had occasional headaches, they were less frequent and less severe than before. The distortions previously noticed had disappeared, and the patient found for the first time that he was able to follow the flight of a ball in a ball game. No change in the correction was made. The patient reported once more, three months later, when he stated that the improvement had continued. The measurements on the space eikonometer were essentially the same as before except for a slight increase in the measured declination error. The final prescription arrived at incorporated, aside from the refractive correction and the prisms, 2.00% meridional magnification, axis 135, for the right eye and 2.00% meridional magnification, axis 45, for the left eye.

It must be pointed out that the various factors involved in this case were corrected in steps and that the patient obtained relief only after the declination error had been corrected by oblique meridional size lenses. The vertical heterophoria was undoubtedly of importance in his visual problem. But that it was not the chief cause of the trouble is borne out by the patient's failure to obtain relief from the prisms alone. In fact, it may be assumed that the improvement in his binocular cooperation brought about by the prisms made the aniseikonic error all the more difficult to cope with. This is indicated by the increase in spatial distortions noticed by the patient while wearing the prisms.

The existing cyclophoria may account for the fact that the declination error was not measured to the full, theoretically expected, amount.

In general, the difficulties encountered in the correction of astigmatic errors at oblique axes can be largely minimized by including an aniseikonic correction in the oblique axis. In some cases, as in the one which will be reported next, the patient is totally unable to wear the oblique refractive astigmatic correction for any length of time.

CASE 8—Mrs. E. W. P., a housewife aged 22, had ulcers of the cornea at the age of about 6 years and had had a great deal of trouble with her eyes. After only a few minutes of reading or sewing severe eye-strain, frontal headaches and nausea occurred. The patient was unable to watch more than half a moving picture without severe discomfort. She had had numerous refractive corrections, several in the two years prior to examination on the space eikonometer, she had also had an aniseikonic correction based on standard eikonometer measurements—all to no avail.

Refraction and Visual Acuity—The results of refraction were as follows:

Right eye $+1.25$ D sph $\square -0.50$ D cyl, axis 170, vision 20/20+

Left eye $+3.25$ D sph $\square -5.00$ D cyl, axis 25, vision 20/30+

At 20 feet (6 meters) there were 1 to 2 prism diopters of exophoria and $\frac{1}{2}$ to 1 prism diopter of right hyperphoria, and at 16 inches (40.6 cm), 6 to 7 prism diopters of exophoria and $\frac{1}{2}$ to 1 prism diopter of right hyperphoria. Examination for stereopsis showed fusion but no depth perception. Except for a fine superficial nubecula of the right cornea and some fine, old superficial maculas of the left cornea, both eyes were normal.

The patient could not tolerate the refractive correction for even a few minutes. Nausea and a pulling sensation in the eyes set in as soon as she put the glasses on. With one eye closed she had no such symptoms. Measurements on the space eikonometer were finally arrived at as follows:

Axis 90 (right) $2.25\% \pm 0.75\%$

Axis 180 (left) $0.50\% \text{ to } 1.00\% \pm 0.50\%$

Measured declination error, δ_m $-1.00^\circ \pm 0.30^\circ$

Computed declination error, δ_c -1.59°

The patient was given overnight the following equivalent aniseikonic correction:

Right eye 3.00% meridional magnification, axis 155
Left eye 2.00% meridional magnification, axis 25

The correction was given in fit-over lenses for her refractive correction. The patient was able to wear this combination with reasonable comfort, and even to read for some time. In the course of the next two days repeated readings were made on the space eikonometer, with the result that the following correction was found which corrected the false appearances of the space eikonometer elements and allowed her to wear the glasses with so much comfort that she could read for two hours.

Right eye $+1.25$ D sph $\square -0.50$ D cyl, axis 170 $\square 2.75\%$ over-all magnification $\square 0.75\%$ meridional magnification, axis 170

Left eye $+3.25$ D sph $\square -5.00$ D cyl, axis 25 $\square 4.00\%$ meridional magnification, axis 45. The patient

has had these glasses for five months but was unable to come for reexamination, owing to an intercurrent illness

Although a final judgment cannot be arrived at, since the patient has not been able to return for examination, this case shows that it is possible to enable a patient with an extreme astigmatic anisometropic refractive error to wear his glasses by correcting the declination error which is introduced by the spectacles. For theoretic reasons this is particularly interesting in cases in which the astigmatic error at the oblique axis is equal and symmetric in the two eyes.

CASE 9—Mrs V C H, the wife of a farmer, was 49 when she was first seen at the Dartmouth Eye Institute. She complained of eyestrain, to which she had been subject since she was a child, burning of the eyes, and frontal headaches. She had worn glasses since the age of 20. In the past years the eyes had burned less and she had fewer headaches, but she was still unable to read for more than five minutes without discomfort.

During 1937, 1938 and 1939 she was given a number of refractive and aniseikonic corrections, without incorporation of corrections at oblique axes, none of which proved helpful. The last correction was as follows:

Right eye +500 D sph —175 D cyl, axis 60
Left eye +475 D sph —175 D cyl, axis 115 —125% over-all magnification. Additional correction for near work of +200 D sph was given for each eye.

The patient returned one and a half years later. At that time the refraction and visual acuity were as follows:

Right eye +550 D sph —175 D cyl, axis 60, vision 20/20-2

Left eye +500 D sph —175 D cyl, axis 120, vision 20/20-3

At 20 feet (6 meters) there was 5 to 6 prism diopters of esophoria, and at 16 inches (40.6 cm), with an addition of +200 D sph for each eye for reading, there was 2 to 3 prism diopters of exophoria. Examination for stereopsis revealed 100 per cent depth perception with the graduated Keystone DB6 chart.

Measurements on Space Eikonometer—The measurements for aniseikonia were as follows:

At axis 90 (right) 0.50% ± 0.25%

At axis 180 (right) 0.50% ± 0.25%

Measured declination error, δ_m +0.85° ± 0.20°

Computed declination error, δ_c +1.70°

The patient was given the following equivalent aniseikonic correction in temporary form:

Right eye +550 D sph —175 D cyl, axis 60 —100% meridional magnification, axis 50

Left eye +500 D sph —175 D cyl, axis 120 —250% meridional magnification, axis 140

For close work a +200 sphere was added for each eye. The patient wore these glasses with great comfort for three months, after which time reexamination yielded essentially the same result as did the first examination, but the axes of the meridional size lenses were shifted to axis 60 in the right eye and to axis 150 in the left eye. The improvement continued, and the patient was given permanent glasses. Three months after receiving the permanent correction the patient was

reexamined on the space eikonometer, and the declination error, δ_m , was found to be 0.00 ± 0.16 degree. She has worn the permanent glasses with great comfort for over a year.

We think that this case is of particular interest not only because it shows close agreement between the measured and the computed declination error and because good results were obtained with the oblique aniseikonic correction, but particularly because the refractive correction for this patient was entirely symmetric except for an insignificant amount of anisometropia in the spherical part.

As has been pointed out in the introduction of this paper, it is generally recognized that oblique astigmatic corrections often are not tolerated well by the patient. Various reasons have been given for the discomfort. Recently Sugar^{25a} reported that many patients whose refraction is accurately determined in monocular vision are uncomfortable in binocular vision. In all 4 cases which Sugar reported a large oblique anisometropic astigmatism was present. He advocated the use of the "spherical equivalent," a technic which apparently makes for visual comfort at the expense of visual acuity. In commenting on Sugai's paper, O'Neill²⁶ and Lebensohn²⁷ pointed out that the anisometropic astigmatic corrections introduce a differential prismatic effect at the reading level, and they claimed that this is responsible for the patient's discomfort. Sugai,²⁸ in replying to these comments, stated that the prismatic differential effect of the glasses could not have played a part since the trial lenses were properly centered before the eyes and the test chart was 6 meters away. This statement, of course, is irrelevant to the problem.

The differential prismatic effect is undoubtedly a factor at the reading level, but we believe that the most important factor in the patient's comfort is the correction of the aniseikonic error produced by cylindric spectacle lenses. All the patients whom we have seen have had difficulties in distant vision, as well as in close work. Our contention is strengthened particularly by instances such as case 9, in which the spectacles contain symmetric lenses which do not introduce a differential prismatic effect at the reading level.

25a Sugar, H S. Binocular Refraction with Cross Cylinder Technic, Arch Ophth 31:34 (Jan) 1944.

26 O'Neill, H. Binocular Refraction with Cross Cylinder Technic, Correspondence, Arch Ophth 31:267 (March) 1944.

27 Lebensohn, J. E. Binocular Refraction with Cross Cylinder Technic, Correspondence, Arch Ophth 31:268 (March) 1944.

28 Sugar, H S. Binocular Refraction with Cross Cylinder Technic, Arch Ophth 31:269 (March) 1944.

SUMMARY AND CONCLUSIONS

The discomfort experienced by patients who require an astigmatic correction at oblique axes appears to be a problem which is as old as modern refraction itself. Various explanations have been offered, both for the patient's asthenopic symptoms and for the spatial distortions caused by such corrections, but no means of relieving them effectively has been suggested in the past.

In this paper we have pointed out that the problem here is essentially the problem of aniseikonia, in particular one that involves a meridional aniseikonia at an oblique axis.

An aniseikonic correction at an oblique axis can be determined if, in addition to the usual measurements for the image size differences in the vertical and the horizontal meridian, a measurement of the declination error introduced by the aniseikonic error at the oblique axis is also obtained.

The term declination error designates a small angular deviation between the images in the two eyes of a vertical line in space. Such a deviation may be the result of the correction of astigmatism at an oblique axis, for this correction would introduce a meridional magnification or elongation of the dioptric image on the retina at an oblique axis. Associated with that magnification is a small rotary deviation of the images of vertical objects. This deviation, when existing between the images of the two eyes, would cause a particular stereoscopic spatial distortion. Under test conditions in which empiric factors to spatial localization are excluded, the declination errors can be measured by the spatial distortion associated with them. The declination error which might be expected to exist in the individual case on the basis of the astigmatic correction can be theoretically computed.

The space eikonometer is an instrument for measuring the declination error, as well as the image size differences in the horizontal and vertical meridians by means of the incorrect binocular spatial localization associated with the aniseikonia. From these measurements the aniseikonic correction involving a meridional correction at an oblique axis can be determined.

A study of the benefit which patients might derive from aniseikonic corrections at oblique axes was made. This paper presents the report on a first group of patients to whom such prescriptions were given. While many problems of a theoretic and practical nature remain to be solved, we feel justified in presenting the results obtained at this time.

Seventy-six patients were given prescriptions for aniseikonia at oblique axes on the basis of measurements on the space eikonometer. The data on 13 patients had to be discarded for lack of information or because of unusual complicating factors, of the remaining 63 patients, 36 were relieved of their symptoms by the correction to a notable degree, 16 were partially relieved, and 11 derived no benefit at all. This high percentage of positive results we consider significant, especially in view of the fact that the patient material was highly selected. The majority of these patients had asthenopic symptoms more severe than has the average patient. Others had ocular and extraocular factors that made a positive result often questionable, even prior to the examination.

Not for all patients did the measured declination error agree in amount and direction with that to be expected on the basis of the astigmatism. For many patients the measured declination error was smaller than the error theoretically expected, for others it was greater. Again, for others it was even in the opposite direction. Nevertheless, patients were helped by the correction of the measured declination error. Other patients had a spherical refractive correction or were even emmetropic, so that the computed declination error was zero. Notwithstanding this, these patients were rendered more comfortable by the correction based on the measurements.

For the time being there are two possible explanations for the measurements in such cases. Either the patients have an oblique basic aniseikonia which is not optical in origin, or they have a cyclophoria. Further research is required to solve this problem. A similar explanation must apply in the case of patients who have a large astigmatic error at oblique axes but for whom no declination error can be measured.

In several patients no relief was obtained by the correction, in spite of the fact that a definite declination error was measured and that it agreed well with what might be expected.

The correction of meridional aniseikonia at oblique axes is particularly helpful in cases in which the patient is absolutely unable to wear an oblique cylindric correction at oblique axes and yet his symptoms necessitate the wearing of such a correction.

The symptoms in these cases cannot be entirely due to a differential prismatic effect of the glasses. This is evident in cases of symmetric refractive errors in which the correction of the declination error afforded considerable relief. It

also follows from the cases in which relief was obtained by correction of the measured declination error which was the opposite of that which might be expected. In these cases the equivalent aniseikonic correction would tend to increase the differential prismatic effect of the glasses.

Mr Leo F Madigan assumed the responsibility of conducting the space eikonometer tests, and through his careful and patient approach to the work this study was made possible.

ABSTRACT OF DISCUSSION

DR LAWRENCE T POST, St Louis. My studies on aniseikonia made personally in more than 450 patients and less personal on about 700 patients during the past ten years have been concerned with practice rather than theory. The figures which my associates and I have obtained indicate that about 80 per cent of patients for whom aniseikonic glasses were ordered definitely helped and that almost 50 per cent were made entirely comfortable. Replies were solicited only from persons who had worn their aniseikonic correction for at least nine months. The first 100 replies to the questionnaire were used for the report which was published in the *Southern Medical Journal* in July 1942, page 649. The first question which arises is whether the major factor in this increased comfort is the correction of aniseikonia or something else, such as a change in the refractive correction made at the time the eikonic lenses were given or the psychologic effect of the elaborate examination. It may also be asked whether the patient could have been relieved by some procedure other than the giving of the eikonic glasses, for example, orthoptic training. I have the impression that the eikonic correction is by far the most important factor in producing this increased comfort. It is not only possible but probable that some of these patients could have been helped by means other than aniseikonic lenses. I must add, however, that patients who, judging from our careful histories and ophthalmic examinations, probably had some additional pathologic condition, such as sinusitis or an anomaly of the extraocular muscles, which caused the symptoms were referred for care of these conditions before being given eikonic glasses.

But I cannot refrain from asking, "What difference does it make whether the discomfort is primarily aniseikonic or muscular or psychic, if wearing of the eikonic glasses results in comfort? Why should one not as well give relief by the simple expedient of prescribing eikonic lenses as by an extensive course of orthoptic training?" To consider the more immediate problems presented by the authors, any one who has worked with aniseikonia has felt the need of an instrument that could measure this error. Perhaps ophthalmologists had not visualized the eikonometer as a possible means of giving comfort to the specific group of patients with astigmatism at

oblique axes the correction of which did not produce comfort, so much as of helping patients with aniseikonia in an oblique plane which has a cause other than astigmatism. However, the application of the so-called space eikonometer in correction of declinations produced by astigmatism at oblique angles is obvious. The number of patients with such an error is probably relatively small. The ability of the eye to overcome muscular and refractive difficulties is amazing, as is the ability of the brain to tolerate deficiencies of muscles and dioptric systems. Thousands of people must have aniseikonia and uncorrected errors of refraction which do not inconvenience them. Probably increasing visual skills would help not only many patients who suffer from aniseikonia but many who have other ocular disabilities. Even granting this premise, most people do not have the time, the energy, the money or the inclination to train these skills, and for them, as well as for the great majority who could not be helped by such training, there will continue to be a need for refractive and eikonic corrections. The authors, in addition to presenting a beautiful theorem, have added a practical method of making a small group of patients comfortable. Aniseikonia can never be fully evaluated clinically or the eyes attain their maximum usefulness until two conditions have been fulfilled: first, the test must be made available to every ophthalmologist, and, second, the cost of eikonic lenses must not be prohibitive to the average patient.

DR ERNEST A W SHEPPARD, Washington, D C. Early students of modern refraction and of ocular motility recognized deviations of the vertical meridians of the eyes. Stevens designated such a deviation as the declination error, and he and Savage emphasized its importance as a cause of asthenopia. The types of declination errors were not clearly understood, and therefore the treatment was unsatisfactory. The authors have described three types, on the basis of the etiologic factors: 1. Declination errors produced by cylindric lenses at oblique axes. In this type the degree of error is variable, being maximal when the meridian of the power of the lens is at 45 degrees or at 135 degrees. It is not amenable to correction surgically. It can be calculated mathematically, but the calculated amount does not always agree with the measured amount because of the influence of type 3. 2. Deviation errors associated with cyclophoria. In this type the degree of the declination error is the same in all meridians and therefore cannot be corrected by lenses. 3. Deviation errors associated with basic meridional aniseikonia. This type may exist with emmetropia or isometropia. It may influence the calculated amount in the first type, so that the measured amount may be less, may be zero or even of the opposite kind. If the declination error is sufficiently large to be recognized in the synoptophore, it should be made a

part of the orthoptic status. Certainly, ophthalmologists and orthoptic technicians should be familiar with the types. For diagnostic purposes it is more important to know the type than the degree. It is unfortunate that disturbances of ocular motility are more often treated according to degree than to type. Using the Ames space eikonometer, the authors have measured the declination error by the spatial distortion associated with it and have corrected it with *iseikonic* lenses. It is an important advance both in refraction and in ocular motility to have recognized the association of the two conditions. The results they have obtained are most gratifying. Most of the patients who come to the aniseikonia clinic have tried about everything to get relief. Many have suffered so long that they have acquired what is usually considered a neurosis. A careful history and examination will often reveal associated ocular, physical and psychologic factors. It is reasonable therefore that not all patients will be relieved by the *iseikonic* correction. The authors have recognized and correctly interpreted the fundamental problem of declination errors, classified them according to the etiologic factors, described an instrument for their measurement and reported results in the correction of such errors by *iseikonic* lenses. They recognize further problems presented by the solution of this one. Another aid has been added to the means of solution of the difficult problem of obstinate asthenopia.

DR HERMANN M BURIAN, Hanover, N H
I wish to thank Dr Post and Dr Sheppard for their thorough discussions. Dr Post stated that a

change in the refractive correction may be a source of relief for the patient. Of course, Professor Ogle and I have considered this. The table gives the pertinent information on the 63 patients on whom the study is based, including the refractive correction worn and the refractive correction prescribed. This will allow every one to judge for himself whether, and to what extent, this factor is of significance. The bearing on the results of the ability to overcome certain ocular difficulties, i.e., of the ability to adapt, is also discussed at length in the paper. I concur most heartily with Dr Post's conclusions. I have maintained for years that if aniseikonia is as important as it is thought to be, its measurement should be so simplified as to enable any one to determine the aniseikonic error with the other ocular anomalies. This is not so simple as it sounds. Numerous difficulties had to be overcome. We have, however, in the past year succeeded in constructing a small instrument, based on the principle of the vectograph, which utilizes the test pattern of the space eikonometer. It is hoped that with this instrument, which should become available as soon as the present difficulties in obtaining materials are removed, the measurement of aniseikonia will be no more difficult than is, for example, the subjective determination of the axis and the amount of astigmatism. We expected to demonstrate a model at the present session, but this was not possible, for lack of space.

Dartmouth Eye Institute

HETEROCHROMIA SYMPATHICA

P H BOSHOFF, MD, AND J J THERON, MD
JOHANNESBURG, SOUTH AFRICA

In a recent publication Hess¹ called attention to certain aspects of heterochromia sympathica in addition to the features usually described. He stressed the presence of status dysraphicus, which is evidence of involvement of the spinal cord and which may present the following clinical signs: (a) signs of localized muscular atrophy, (b) reflex abnormalities, (c) vasomotor changes, (d) disturbance in function of the urinary bladder and of the bowels, (e) abnormalities in the distribution of the fat of the body and (f) scoliosis. In accordance with von Herrenschwand's suggestion,² heterochromia sympathica became recognized as a separate clinical entity. Extraocular involvement of the sympathetic nervous system in this condition is not unknown. Mayou³ recorded a case of heterochromia sympathica following birth injury to the sympathetic system. Waardenburg,⁴ Metzner and Wolfflin⁵ and Bistis⁶ described involvement of the facial nerve and cervical portion of the sympathetic trunk (Horner's syndrome and hemiatrophy) in association with heterochromia sympathica. Cases have been recorded in which injury of the cervical portion of the sympathetic trunk by trauma⁷ or at operation⁸ was followed by heterochromia. This occurred in young persons below the age of 25 years. Passow⁹ first associated heterochromia with skeletal and cranial structural anomalies.

There is enough evidence to show that with a certain type of heterochromia¹⁰ the sympathetic

1 Hess, L. Heterochromia of Iris, Arch Ophth 30 93 (July) 1943

2 von Herrenschwand, F. Klin Monatsbl f Augenl 60 467, 1918

3 Mayou, M S Tr Ophth Soc U Kingdom 36 410, 1916

4 Waardenburg, P J Nederl tijdschr v geneesk 1 22, 1929

5 Metzner and Wolfflin Arch f Ophth 91 167, 1916

6 Bistis, J Ztschr f Augenh 82 180, 1934

7 Lazarescu, D, and Lazarescu, E Ann d'ocul 170 767, 1933

8 Bistis, J Ann d'ocul 45 569, 1928

9 Passow, A Arch f Augenh 108.137, 1933

10 W S Duke-Elder (Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1938, vol 2, p 1403) classifies heterochromia thus (1) simple heterochromia, (2) complicated heterochromia, (a) heterochromia cyclitis and (b) sympathetic heterochromia

nervous system is involved. Four cases which may be of interest are here described. Because we have seen so few cases of heterochromia sympathica (4 in a series of 13,450 cases) and because there was evidence of birth injury in 2 of them, we consider our cases worthy of record. It is noteworthy that among the 13,450 cases observed by us in South Africa, not 1 instance of heterochromic cyclitis was encountered. Seventeen cases (in the series of 13,450 cases) of simple heterochromia are on our records. Although we observed between 3,000 and 4,000 South African Negroes, not 1 case of heterochromia simplex or heterochromia complicata was seen.

Of our 4 cases of heterochromia sympathica the condition followed birth injury in 2, sympathetic disturbances became evident soon after birth in the third, and changes in color of the iris occurred during the patient's lifetime in the fourth.

REPORT OF CASES

CASE 1—T W B, a man aged 31, stated that he was born "with his head twisted on to his left shoulder." Delivery was by forceps extraction. He had an oblique linear scar on the right side of his forehead and another over the right parietal region of his scalp. The iris of the right eye was brown, and that of the left eye was blue with a few brown specks in it. The right palpebral fissure was 2 mm wider than the left. The diameter of the right pupil was 3.5 mm, and that of the left pupil, 2.5 mm. The skin of the left side of the forehead and the eyelids was continually wet with perspiration throughout both summer and winter. No perceptible differences were to be seen in the fundi. Refractive errors required the following correction: right eye, -0.5 D sph \supset -0.5 D cyl, axis 180; left eye, -0.5 D sph \supset -1.5 D cyl, axis 180. With correction visual acuity was 6/6 in each eye.

CASE 2—J H D, a sergeant aged 38, stated that his was an "instrument birth" from which he retained a depression in the bone on the left side of his forehead and a scar over the right side of his lower jaw opposite the second premolar tooth. The color of the right iris was blue, and that of the left iris, light brown. The right palpebral fissure was narrower than the left. The diameter of the right pupil was 2.5 mm, and that of the left pupil, 3 mm. The fundi did not differ from each other. Refraction showed rather mild simple hyperopic astigmatism with horizontal axes in each eye. No abnormality in function of the skin was seen.

In both these cases the physician reported that no other signs of sympathetic involvement

existed. There was no family history of heterochromia. In these 2 cases the cervical sympathetic fibers must have been damaged at birth, with the result that the disparity in color of the iris developed.

CASE 3—S C van W, a boy 6 years of age, had a normal birth and infancy. There was nothing of importance in the family history. From infancy the left side of his face down to the chin became flushed at times of exertion or emotion. The cornea of the left eye was 0.5 mm larger than that of the right eye in both the vertical and the horizontal diameter. The left pupil was larger than the right. The iris of the left eye was brown, and that of the right eye was blue. The palpebral fissure of the left eye was wider than that of the right eye. No abnormality in function of the sweat glands or in general constitution could be found by the pediatrician. With a +0.75 D sphere for the right eye vision was 6/6 in that eye, and with an 8 D sphere for the left eye vision was barely 6/60 in that eye. The left eye was congenitally amblyopic.

In this case no skeletal differences existed, but there was obviously an imbalance of sympathetic function on the two sides of the body, probably of congenital origin.

CASE 4—H W, a man aged 45, had an interesting history of changes in the color of his irises. His family history revealed no clues to account for this condition. He stated that his health had always been exceptionally good, but he had had thorough internal medical and roentgenologic examinations for the presence of any possible condition, such as unilateral silicosis or tuber-

crosis,¹¹ which could have caused a disturbance of the sympathetic nervous system. None had been found. His complexion for a European born in England, and in spite of the fact that he was an underground worker in a South African gold mine, was singularly ashen brown. I examined his old military papers, the first of which, dated June 24, 1916, stated "Color of eyes, light gray." He offered the information that a short time after this record was made his friends told him that the color of his eyes had changed. He himself had noticed it. The second certificate, dated Oct 12, 1918, stated "Color of eyes, brown." I saw him in January 1942, when the right eye was blue and the left eye was brown. No other differences were noted between the two eyes. He stated that the latest change in color of the irises (heterochromia) had taken place gradually during the last fourteen years.

We are at a loss to explain the mechanism in case 4, but we regard the condition as heterochromia sympathica because of the changes which the color of the irises seemed to have undergone during the patient's lifetime. There is, of course, the possibility that the earlier examinations of the eyes were made in a haphazard manner, that is, only one eye may have been looked at on each occasion. However, such changes in color of the iris may occur, and the recording of this case may bring forth descriptions of other cases of similar nature in which other causal factors exist.

6 and 7 Mariners, Jeppe and Joubert Streets

11 Giamantoni and Possente Ann di ottal e clin ocul 61 823, 1933, cited by Duke-Elder¹⁰

Clinical Notes

PLASTIC CORNEAL BATH FOR APPLICATION OF PENICILLIN

CAPTAIN HUGH A G DUNCAN, ROYAL CANADIAN ARMY MEDICAL CORPS

Recent work by von Sallmann and Meyer¹ has indicated that penicillin is of little value in the treatment of intraocular infections if given intramuscularly or instilled as drops. Their results suggested that iontophoresis and the use of a corneal bath plus a wetting agent are the only satisfactory means of introducing a sufficient

concentration can be obtained. The latter method is, moreover, much easier to carry out, especially for ophthalmologists in service.

A simple corneal bath of plastic (acrylic acid derivative) has been devised, with the technical help of Major J M McDougall, Canadian Dental Corps, and his assistant, Sgt H Travels. It is modeled from an average-sized contact lens. The corneal curvature is made greater than that

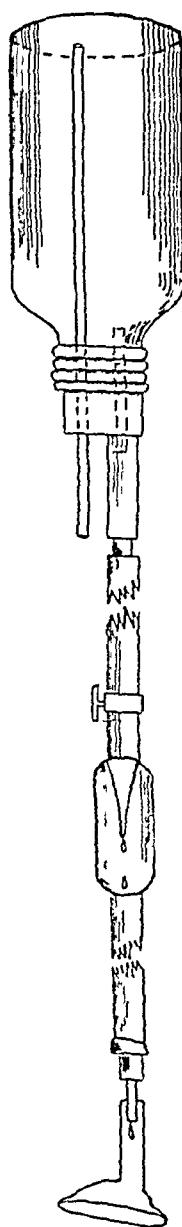


Fig 1—Plastic corneal bath

concentration of penicillin into the anterior chamber. According to their report, iontophoresis is more effective, but with the corneal bath an ade-

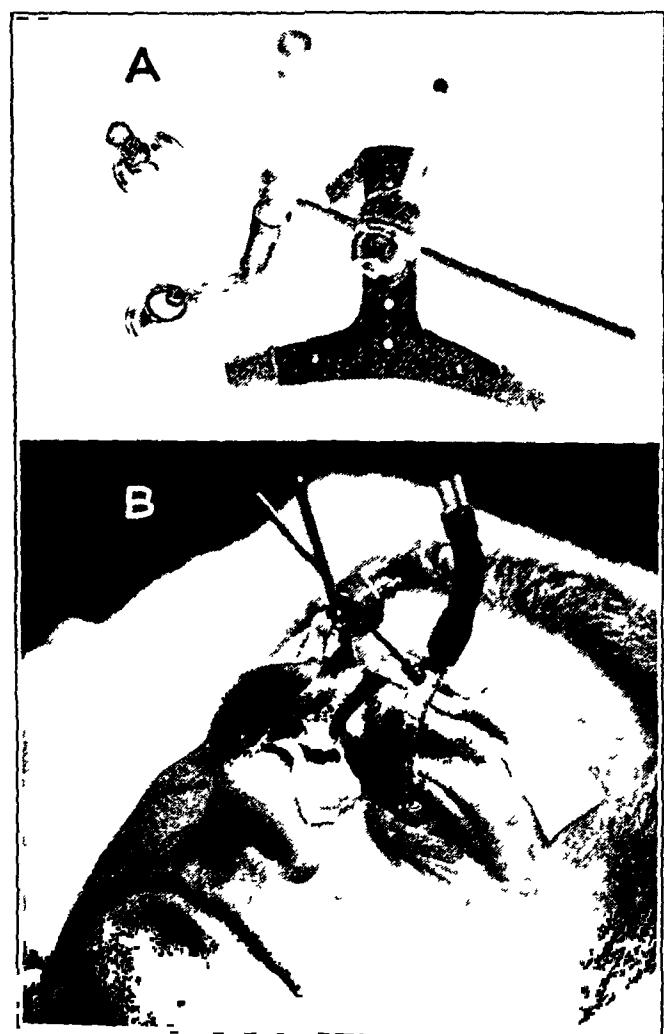


Fig 2—Photographs of the plastic corneal bath

of an ordinary contact lens. A plastic tube is molded in place between the apex and the scleral gutter at an angle of 20 degrees with the antero-posterior axis. The tube is placed below the apex in order that when the lids are closed and the eye turns up the dome may not be displaced from the cornea. The angle of the tube is such that when the patient is on his back the tube is vertical thus with the drip method to be

From the Canadian General Hospital no 4

¹ von Sallmann, L., and Meyer, K. Penetration of Penicillin into Eye Arch Ophth 31 1-7 (Jan) 1944

described, the tubing does not drag on the plastic inlet to the bath (fig 2)

If a constant bath is desired, a dip can be arranged from an ordinary set for continuous intravenous infusion, with the tubing suspended vertically. No weight is placed on the bath. A gutta-percha ring can be placed around the tubing above its outlet, to prevent the tip from striking the cornea if the tubing should fall accidentally. With many types of sets for intravenous infusion this adaptation is unnecessary.

For this bath, as well as for the drops, I have used penicillin in a strength of 1,000 units per cubic centimeter, rather than the more common concentration of 500 units per cubic centimeter, because experimentally it has been shown that the stronger concentration remains effective at ward temperature for three to four days. The weaker concentration remains effective for less than half that time.

In using the apparatus described here, one must be careful not to leave it in a badly inflamed eye too long because of the danger of pressure necrosis. The patients with whom I have used this bath bore it with comparative comfort. Nupercaine hydrochloride was added to the penicillin, as suggested by von Sallmann and Meyer.

I have not yet had sufficient experience to warrant definite conclusions as to the optimum frequency or duration of the treatments. However, from clinical experience with iontophoresis of penicillin, I believe that daily baths for comparatively short periods may be satisfactory, especially when they are supplemented with intramuscular administration of penicillin.

This article is published at the suggestion of Lt Col R E Wright, Indian Medical Service, who gave valuable advice; it is felt that a suitable corneal bath may be of material aid in the treatment of war injuries with resultant intraocular infection.

Correspondence

BILATERAL INFANTILE GLAUCOMA ASSOCIATED WITH BILATERAL CONGENITAL HEMANGIOMA

To the Editor.—A recently recorded case of "bilateral infantile glaucoma associated with bilateral hemangioma congenital (nevus flammeus)" (ARCH OPHTH 32: 214 [Sept] 1944) has come to my attention. The author, A. M. Rodicina, states that a review of the literature failed to reveal any case of a similar condition. I should like, therefore, to suggest that the following cases of similar nature have been reported and listed by J. Ringland Anderson, in his monograph entitled "Hydrocephalus or Congenital Glaucoma" (London, Cambridge University Press, 1939). These cases are listed as instances of bilateral hydrocephalus and bilateral facial nevi (Beltman, J. Arch f Ophth 59: 502, 1904; Marchesani, O. Wien med Wochenschr 75: 2538, 1925; Horay, G. Zentralbl f d ges Ophth 20: 793, 1929; Dunphy, E. B. Am J Ophth 18: 714, 1935; Perera, C. A. Bilateral Buphtalmos Associated with Naevus Flammeus, ARCH OPHTH 14: 626 [Oct] 1935; Fleischer, B. Klin Monatsbl f Augenh 61: 152, 1918).

It is presumed that by the term infantile glaucoma the author means a primary type of congenital glaucoma, or hydrocephalus, which according to Anderson's definition would include the case under discussion. Besides these cases listed by Anderson, 4 cases in which the condition was considered as "bilateral glaucoma (other than congenital) with bilateral facial nevi" have been recorded, and in all these cases glaucoma had developed before the age of 20 years. They are Biro's case, with onset at 8 years, Knapp's case, with onset at 4 years (mild hydrocephalus?), Horay's case, with blindness at 19 years, and Mehney's case, with blindness at 20 years. Since the condition in the author's case appeared between the ages of 9 and 11 years and since the diameter of the right cornea was 13 mm and that of the left cornea was 11 mm it appears that hydrocephalus was present in the right eye, but probably not in the left eye. Accordingly, in the sense intended in the report, the glaucoma in the left eye was probably not of the true congenital type, so other cases of this type, in which bilateral facial nevus coexists with secondary glaucoma, or the pseudoglaucoma of Ballantyne (Brit J Ophth 14: 481, 1930, 24: 65, 1940), may also be noted.

It may be mentioned at this time that of 60 cases of hydrocephalus associated with facial nevi, 35 per cent showed bilateral nevus

Again, it may be interesting to point out that in Anderson's series, the hydrocephalus was bilateral in 85 per cent of cases. From this one would assume that if the patient had bilateral nevus, he would be more than likely to have bilateral glaucoma. Yet in all cases of hydrocephalus with facial nevi (60 cases) bilateral glaucoma was present in only 13 per cent. Does this indicate that the cases have not been followed to a conclusion, or does it suggest an element of prognosis? Is the relation of facial nevus to hydrocephalus of no significance? May not the facial nevus be related to a glaucoma of delayed development, which occasionally appears as hydrocephalus very early in one eye and as another type of glaucoma later in the second eye, modified in character by changes occurring during the growth and development of the eye?

The author states that "roentgenograms of the skull indicated no pathologic change in the sella turcica." I believe there have been reported only 3 or 4 cases of this condition in which changes were observed in the pituitary gland, and in these cases no relationship between the angioma and the changes in the pituitary was apparent. It would seem to be more important to make roentgenograms of the skull for the presence of calcification, particularly of the occiput, for angiomas of the meninges, cortex and cerebellum may be present. The relationship between cutaneous nevus in the distribution of the trigeminal nerve and angioma of the occiput, both meningeal and cortical, points to an embryonic anlage. It has been shown that the roentgenographic report for calcification will be negative if the tumor is present but has not as yet become calcified. Anderson has pointed out that glaucoma develops only in eyes with tarsal and conjunctival angiomatosis, and not in eyes in which these appendages are not involved.

EMANUEL ROSEN, CAPT, MC, AUS

RETINAL CHANGES ASSOCIATED WITH DIABETES AND WITH HYPERTENSION

To the Editor.—In his article, "Retinal Changes Associated with Diabetes and with Hypertension," published in the February 1945 issue of the ARCHIVES, Ballantyne presents illustrations showing dilatations of capillaries in the retina which he calls microaneurysms. He states that in fixed preparations "the aneurysms can be clearly seen in greater number than on oph-

thalmoscopic examination" I do not know whether the term aneurysm can properly be applied to a capillary dilatation, but from his illustrations and description there is no doubt that Ballantyne saw numerous capillary dilatations. This is in accord with the assumption which I made in my publication "Problem of Diabetic Retinitis" (ARCH OPHTH 25:139-148 [Jan] 1941) I expressed the opinion that in view of the present understanding of local circulatory disturbances in an organ, "the hemorrhages in the retina must be considered as the result of prestasis, that is, the result of slowing of the blood flow through dilated terminal vessel units" (page 143). Ballantyne's capillary microaneurysms seem to be nothing more than irregularly dilated capillaries presenting a condition of prestasis. Undoubtedly, as Ballantyne says, the dilatations are "the earliest manifestation of diabetic retinopathy" and "should throw some light on the pathogenesis of that condition."

There is, however, no necessity of assuming, as Ballantyne does, that unknown toxic factors are responsible for either the capillary dilatations or the occurrence of the hemorrhages. (Any comparison of human diabetes with diabetes experimentally induced with alloxan should not, of course, be made, the two conditions have nothing in common.) Hemorrhages as a result of diapedesis from capillaries occur whenever and wherever there are dilated capillaries with a condition of prestasis. This is a "normal" pathologic event. Also, in cases of diabetes, even of long standing, especially of the milder form, there are no known toxic factors. The only abnormality in such cases is the hyperglycemia, and this it is, as I have said in my article which stands in a causal relation to diabetic retinopathy and is, in all probability, responsible for the capillary dilatations, or Ballantyne's "microaneurysms."

The changes in the retinal veins mentioned by Ballantyne occur to a notable degree only in a comparatively small number of cases of diabetic retinopathy. Together with formation of new vessels, they characterize the peculiar diabetic retinitis proliferans, the histologic features of which have been described by Klein. Only recently I was shown a case in which the fundus of the left eye was literally filled with a mass of newly formed vessels, while in the fundus of the right eye there could be seen the beginning of such vessel formation, together with hemorrhages and all manner of changes in the veins. The pathogenesis of these changes is more difficult to explain.

Finally I think, one should not compare the changes in the fundus occurring in cases of arterial hypertension with those associated with diabetic retinopathy. Fundamentally, the alterations have nothing in common. The statement that in diabetes the "changes are primarily in the capillaries and venules while in the hypertensive

type they are in the arterioles and precapillaries" is not acceptable.

HERMAN ELWYN, M.D., New York
239 Central Park West

ILLUMINATION FOR OPHTHALMOLOGISTS

To the Editor —In the January 1945 issue of the ARCHIVES, Dr Legrand H. Hardy and Dr Gertrude Rand present a paper entitled "Elementary Illumination for the Ophthalmologist." The scientific specification of foot candles, or intensity of illumination, has been one of the major objectives of researches in seeing for many years, and new knowledge and technics have crystallized in the past decade. The authors treat this important aspect meagerly. In fact, any one familiar with the growth of knowledge pertaining to the relations of illumination to the visibility of visual tasks and the complex relationships of light, vision and seeing knows that much of the progress in this direction has been made since 1931. The authors ignore this fact and quote Troland as of 1931 with a finality that is ridiculous. They might as well ignore the "miracle drugs" which have come into medical practice since that time and all the great progress in medicine, surgery and other sciences and practices of the past decade. They even cite Katz's statement made in 1896! This was certainly the period of antiquity in lighting knowledge and practice, and it approaches a similar period in some major aspects of medical, ophthalmologic and other practices which involve human welfare.

To any one sincerely interested in knowledge of the relationships of light and sight and of the relations of these phenomena to visibility in an extreme variety of visual tasks, many scientific papers are available in appropriate journals published since 1931. The work of my associates and me, which the authors mention casually in passing is ignored, together with all the work of other investigators. The authors should know that our researches in seeing are prosecuted with the same freedom and desire to ascertain the truth as exist in all General Electric laboratories, whose accomplishments speak for themselves. Why do the authors ignore the results of extensive researches of the past thirteen years which are revolutionizing lighting practice and are providing for the first time a scientific foundation for the specification of light and lighting? There may be an answer to this question, but it can scarcely be an excuse for the amateurish and antiquated discussion of the important matter of illumination. Much of the revolutionary knowledge and some of the new criteria, technics and devices have interested many ophthalmologists, who recognize that seeing involves other sciences and practices which affect the efficiency, safety and welfare of human beings throughout the present day artificial world of prolonged critical

seeing. Certainly, human eyes and human seeing machines are entitled to all the help that is available. They will not get it from persons who assume that the growth of knowledge ceased in 1931.

MATTHEW LUCKIFSH

Lighting Research Laboratory, General Electric Company, Nela Park, Cleveland

To the Editor—As Mr Luckiesh has paid no attention to either our title or our references to recent and reliable sources of information on illumination he does not move us to change any statement we have made.

This note gives us the opportunity of correcting a typographic error on page 2 where a reciprocal sign was omitted. There are $\frac{1000}{1076} = 929$ sq cm in a square foot, hence the foot lambert as stated, equals 1076 millilamberts.

LEGRAND H HARDY, M D
AND

GERTRUDE RAND, Ph D

23 East Seventy-Ninth Street, New York

INCOMPATIBILITY OF SILVER NITRATE AND SULFATHIAZOLE

To the Editor—Since the publication of an article by D F Gillette entitled "A New Aid in Removal of Foreign Bodies of the Cornea" (ARCH OPHTH 31: 129-130 [Feb] 1944), my associates and I have been applying a 1 per cent solution of silver nitrate to the site of a foreign body. We agree with the author that the procedure facilitates the removal of metallic foreign bodies embedded in the epithelium.

In 2 of approximately 100 patients so treated a dense, grayish white precipitate has developed in or below Bowman's membrane about the site of the foreign body on application of the silver. In the first patient the area was not in the visual axis. Treatment was conservative, and the lesion epithelialized satisfactorily. During the six months in which the precipitate has been under observation it has faded slightly, but is still conspicuous. Since we had used no other medication except tetracaine hydrochloride and the patient was not taking drugs, we could not explain a similar precipitate which appeared on application of silver nitrate to the cornea of another patient. Two days later, when it was evident that a conspicuous tattoo had been produced, the area was delineated, the cornea split superficially and the precipitate excised. The area healed smoothly, and normal visual acuity was obtained in the eye.

A history was obtained of the previous instillation of sulfathiazole ointment in this eye, as well as in other eyes with embedded foreign bodies which were subsequently treated with silver.

The precipitate dissolved readily in nitric acid and showed a strong reaction to silver. Unfortunately, there was insufficient quantity for further tests.

When 1 per cent silver nitrate is dropped into a saturated solution of sulfathiazole a fine white precipitate forms. Unfortunately, I have not been able to discover the exact nature of this precipitate. However, in a personal communication, Dr Charles Allen Thomas, central research director of the Monsanto Chemical Company, suggests that it is either silver sulfathiazole or the silver salt of aminothiazole.

Partial hydrolysis to aminothiazole or metathesis, with the formation of sodium sulfathiazole, may form intermediate reactions which determine the extent of the precipitation. However, for practical purposes, in the absence of a more specific explanation of the phenomenon, one may assume that a break in Bowman's membrane allows a significant localized absorption of sulfathiazole and the formation of an insoluble precipitate on contact with silver nitrate. In cases in which no break in Bowman's membrane occurs one may assume that there is too little absorption of the sulfathiazole to produce the insoluble precipitate.

Caution should be used in the application of silver nitrate to a cornea in which Bowman's membrane has been broken and which has been exposed to sulfathiazole.

COMMANDER A M CULLER (MC), U S N R

DEFECTS IN THE VISUAL FIELD PRODUCED BY HYALINE BODIES IN THE OPTIC DISKS

To the Editor—In his interesting article entitled "Defects in Visual Fields Produced by Hyaline Bodies in the Optic Disks" (ARCH OPHTH 32: 56 [July] 1944), Dr C Wilbur Rucker presents the changes in the visual fields in 5 cases of hyaline bodies in the optic disk. The fields presented were remarkably similar to each other and to the fields characteristic of glaucoma simplex. Since the author has not drawn attention to this fact, I believe it should be pointed out. In 4 of the 5 cases there were defects in the lower nasal fields, and in 2 cases, Seidel scotomas, examination in case 5 revealed a nasal step in each eye, in case 4, baring of the blind-spots, and in case 3, loss of the nasal fields and ring scotomas. If the field defects were analyzed for the internal isopters by test objects of smaller angles, viz., 1/1,000, 1/2,000, 1/4,000 I believe one would see (1) the ring scotoma ending in a nasal step, (2) a break-through of the Seidel signs to the nasal periphery and (3) additional nasal steps.

The author has presented the fields without drawing any conclusion. I think it should be pointed out that the fields presented are not "the usual varieties of defects in the visual fields caused by hyaline bodies in the optic disks," but are defects produced by any lesion at the nerve head. The fields presented uphold the generalization that a lesion at the optic disk produces peripheral field defects pointing to the disk and are due to lesions in the nerve bundles.

at the disk. Other examples of peripheral field defects produced by a lesion of the disk are glaucoma, choroiditis juxtapapillaris of Jensen, papilledema and arterial occlusion.

The article has bearing on the various views as to the relation of the peripheral and the central retinal fibers as they pass into the papilla. According to Wilbrand and Saenger, and van der Hoeve, the fibers from the periphery of the retina pass to the outside of the nerve, and the peripapillary fibers, to its center. Since the physiologic cup exposes the most central fibers of the disk to pathologic change and since a pathologic process at the disk gives peripheral defects, it is likely that the views of the aforementioned authors are not correct.

I believe Dr Rucker has presented additional clinical evidence in support of the view that the

most central fibers at the disk represent the retinal periphery.

JACK V LISMAN, M.D., New York
654 Madison Avenue

To the Editor —I doubt whether my brief report of visual field defects produced by hyaline bodies in the optic disk contributes anything to knowledge of the arrangement of the nerve fibers in the disk. The hyaline masses are usually so irregularly distributed, and sometimes so deeply buried, that one cannot be certain as to which bundles of nerve fibers they interrupt.

I appreciate the interest of Dr Lisman in this study.

C. W. RUCKER, M.D., Rochester, Minn.
The Mayo Clinic

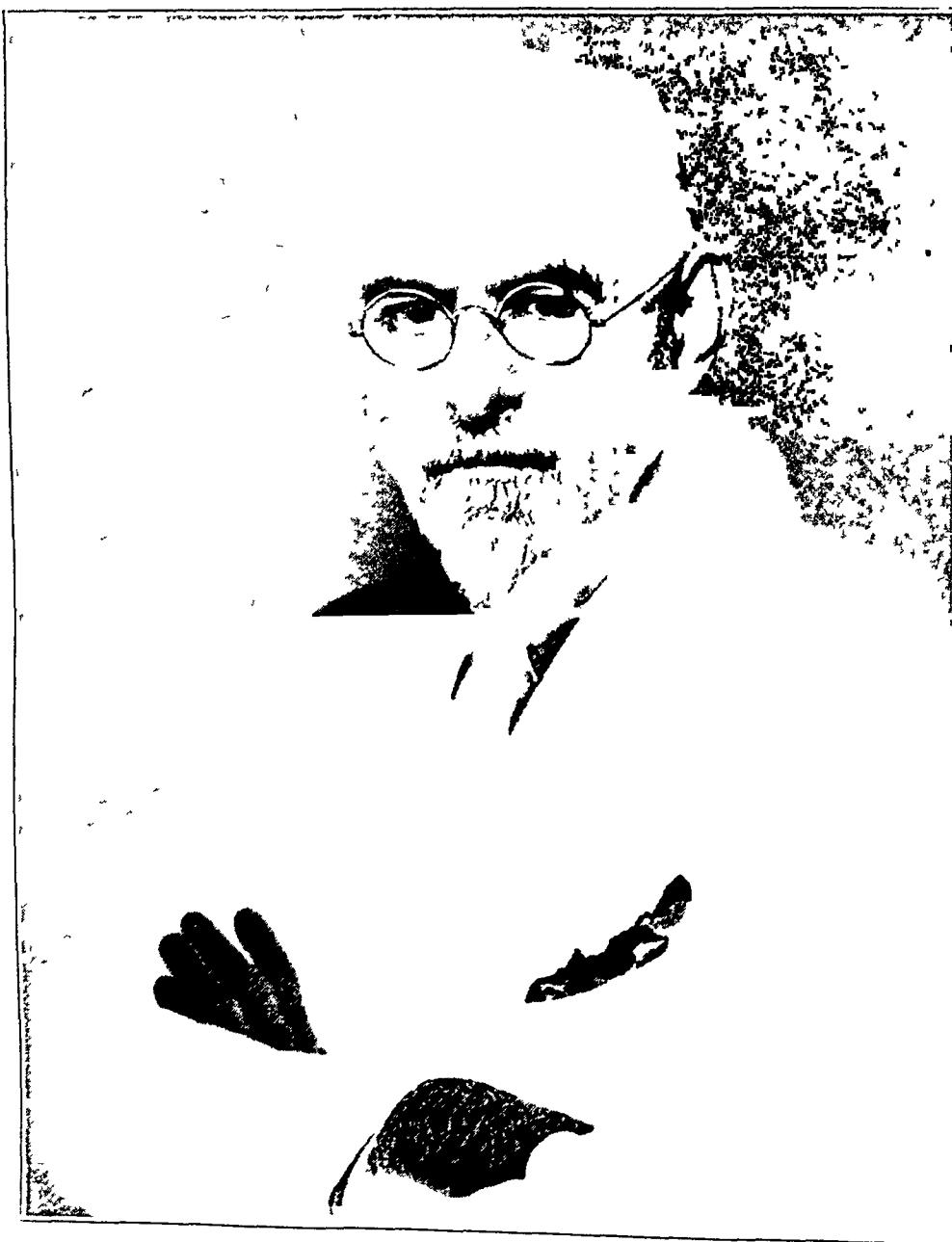
Obituaries

ELLICE M ALGER, M D

1870 - 1945

Dr Ellice M Alger was born in Burlington, Vt., in 1870, and died at the New York Post-Graduate Hospital on Feb 18, 1945, after an illness of several months. He is survived by his widow, Mrs Louise Stevenson Alger, and a brother, George S Alger.

He had been a member of the American Ophthalmological Society since 1915 and was also a fellow of the American College of Surgeons and a member of the New York Academy of Medicine. He was former chairman of the section of ophthalmology of the Academy, as



ELLICE M ALGER, M D
1870 - 1945

Dr Alger was graduated from the University of Vermont in 1890 and from its medical school three years later. He became instructor of ophthalmology at the New York Post-Graduate Hospital in 1902, receiving his professorship in 1912 and retiring in 1938.

well as a former president of the New York Ophthalmological Society.

In his fifty years of ophthalmic practice, Dr Alger published several important papers. During his later years he became deeply interested in conditions relating to industrial oph-

thalmology He was a pioneer in the campaign to improve industrial lighting and in instituting safeguards against oculai hazards in industry In 1915 Dr Alger assisted in the organization of the National Society for the Prevention of Blindness, serving continuously on its board of directors Previously he was a member of the New York Association for the Blind

In 1936 Dr Alger was awarded the Leslie Dana gold medal for his outstanding achievements in the prevention of blindness and the

conservation of vision. This medal is presented annually by the Research Association of Ophthalmology

Dr Alger's kindness and sympathy to clinic patients was significant of his character His students were stimulated in the study of ophthalmology and profited by his practical demonstrations His colleagues admired him for his modesty, friendliness and sincerity

MARTIN COHEN

THOMAS HARRISON BUTLER D M (OXFORD), F R C S
1871-1945

Thomas Harrison Butler, the eminent English ophthalmologist, died suddenly at Hampton-in-Arden, Warwickshire, England, on Jan 29, 1945. He was born at Stanhope, County Durham, England, on March 18, 1871. As the recipient of a scholarship, he entered Corpus Christi College, Oxford, in 1889. Here he won first class honors in natural science, graduating with the degree of Bachelor of Arts in 1893. He qualified from St Bartholomew's Hospital in 1895. The year following he was awarded the Radcliffe Traveling Fellowship of the University of Oxford, which made it possible for him to spend several years in work in the great eye clinics on the Continent. For a time he was plague medical officer at Durban and harbor physician at Port Elizabeth, South Africa. The experience thus gained enabled him to write a thesis on the subject of plague, which won for him his doctorate at Oxford in 1902. For the next four years he served as assistant surgeon to the St John Ophthalmic Hospital in Jerusalem.

On his return to England from Jerusalem, Dr Butler wrote the British abstracts for these ARCHIVES—a task that he carried on for many years. He contributed a number of original articles to this publication, beginning with a paper on the treatment of trichiasis, in 1908.

Dr Butler settled down to the practice of ophthalmology in Coventry and Leamington. His associations with these two cities covered a period of over forty years. His reputation spread far beyond the Midlands, until he became known to the medical profession throughout the English-speaking world.

In 1925 he attended Professor Vogt's course on use of the slit lamp, in Zurich. Two years later he published his book, entitled, "An Illus-

trated Guide to the Slit Lamp." This was the first book on the subject to be written in the English language, and it is as its author that Dr Butler is best known. Being a gifted draftsman, he was able to provide the numerous illustrations in his book himself, and this he did for all his articles, which were many and mostly short.

Dr Butler came to occupy high places in his specialty. To mention by no means all, he was at various times president of the Ophthalmological Society of the United Kingdom, of the ophthalmic section of the Royal Society of Medicine and of the ophthalmic section of the British Medical Association. He had the distinction of being selected to deliver the Doyne Memorial Lecture and the Montgomery Lectures. He was a most active member of the Oxford Ophthalmological Congress from the time of its foundation, serving on its council for many years. He will be sorely missed at its meetings especially by those who came from great distances. It was his habit to single them out and take an interest in them. In recognition of his talents and energy and of the good use that he made of them, the Royal College of Surgeons elected him to the honorary fellowship in 1941.

No sketch of Dr Butler's career would be adequate without mentioning the fact that in the yachting world he was widely known as a designer of small cruising yachts. This was his hobby.

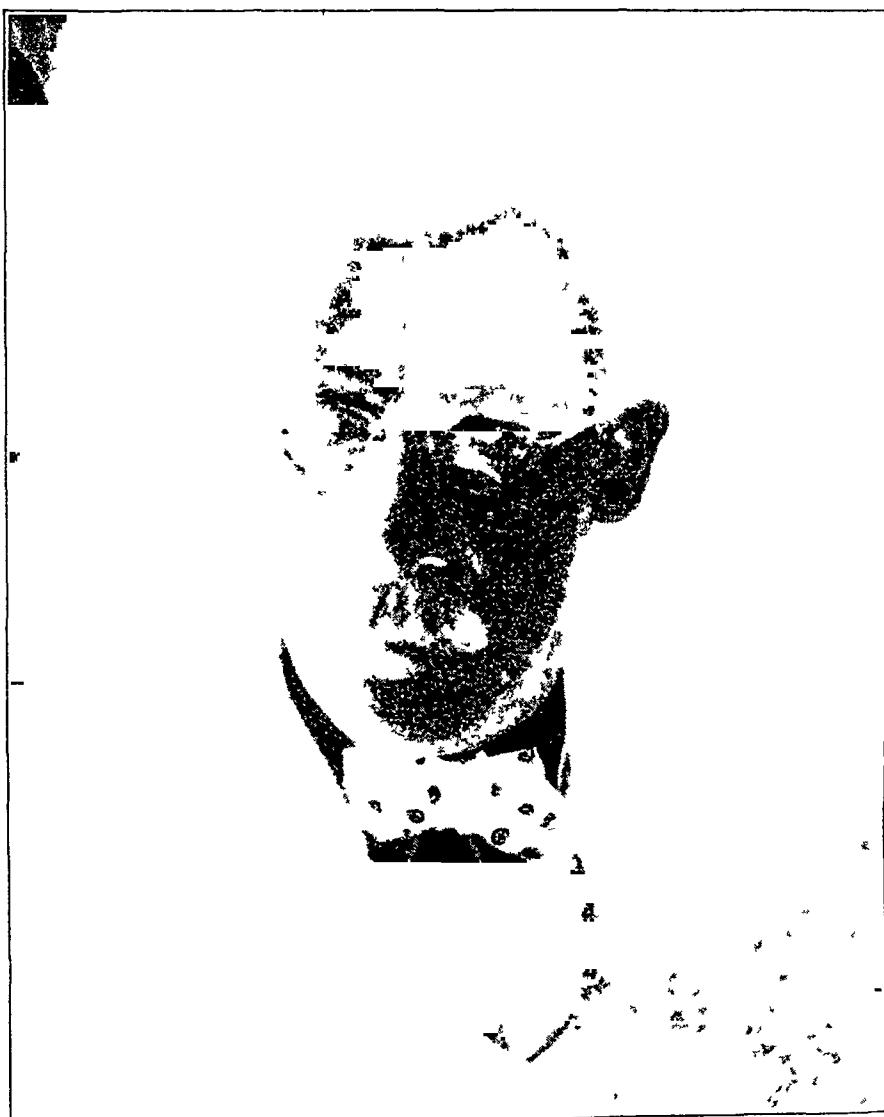
He died in harness. Owing to the exigency of the times, he returned from retirement to take up clinical work in Birmingham, in an endeavor to replace a son who had been called to the armed forces.

BERNARD SAMUELS

MARK J SCHOENBERG, M D
1874-1945

The life of Mark J Schoenberg which ended Feb 15, 1945 in New York after a brief illness, is a brilliant illustration not only of the opportunities that America still offers but of one that was purposeful and rich in accomplishments. He was born in Pitesti, Rumania, on Dec 23, 1874

titioner on the East Side, where house calls were made on a bicycle, at \$1 a visit. He soon showed an inclination toward ophthalmology, was appointed chief of the eye clinic at Mount Sinai Hospital and conducted his own hospital for ophthalmic diseases in lower Manhattan. In



MARK J SCHOENBERG, M D
1874-1945

Seeing the difficulty of his coreligionists in obtaining admission to the city high school, he organized and became a teacher in a new one with more democratic privileges. This training helped him in his later lucid medical writings and teachings. He graduated from the Bucharest Medical University in 1898 and came to this country in 1900. He was first a general prac-

1908 he became connected with the Herman Knapp Memorial Eye Hospital and acted as attending surgeon from 1918 to 1935, when he retired. However, he continued his interest in the glaucoma clinic which he had started in that hospital, as the first in New York. His loyalty to the interests of this institution was outstanding, and he was especially helpful in the all day, six

month postgraduate course which were given for several years after 1918. He was instructor in ophthalmology at Columbia University College of Physicians and Surgeons. In 1919 he was made a member of the American Ophthalmological Society his thesis being entitled "Remarks on Diagnosis and Treatment of Luetic Involvement of the Optic Pathways." He was also a member of the American Academy of Ophthalmology and Otolaryngology and the New York Academy of Medicine and served as chairman of the Section of Ophthalmology of the Academy in 1932 and 1933. He was the founder of the New York Society for Clinical Ophthalmology and acted as its first president, in 1935. He was consulting ophthalmologist to the Bronx Hospital and to the Manhattan Eye, Ear and Throat Hospital, where he was director of the glaucoma clinic. He was chairman of the committee for glaucoma of the National Society for the Prevention of Blindness.

Dr Schoenberg was both loved and respected, loved for his kindness to every one, even those with whom he disagreed, and respected for his scientific accomplishments. He was by nature sensitive, a trait which enabled him to detect early expressions of disease in his patients. He was modest and enthusiastic, in all a highly successful practitioner, always thirsting for knowledge. He labored long before presenting his conclusions, and then gave only facts that were beyond refutation. He emphasized careful, complete history taking in every case, including information on diet and possible psychosomatic relations. He never lost the common touch. His humble and difficult beginning always tied his sympathies with the special problems of the poor patient. He encouraged writing by his assistants, not only by personal help but with monetary rewards. He had a most stimulating curiosity concerning medical facts, he tried to conceive of ophthalmologic problems in the broader light of systemic disorders, and his attitude toward original thought was that no observation or contribution can be too trivial to be worthy of recording.

A review of his forty-six published articles reveals three outstanding features. The first was his attempt to apply preventive medicine by making specialists and general practitioners aware of disease before it has made its inroads. In 1912 he pleaded for departments in hospitals to be devoted to preventive medicine. In 1919 he stated that the early diagnosis of syphilitic in-

vovement of the optic pathways is possible only through routine periodic ophthalmologic examinations of every patient with syphilis from the very beginning of the infection throughout life. From 1912 until recently he labored to be able to detect glaucoma not only in its early phases but even in the preglaucoma stage, through studies on ocular drainage and pupillographic examinations. To him is due much credit for making even the layman conscious of glaucoma.

The second feature was his aptitude for judging valuable contributions of others from abroad and he was the first to utilize them here at home. In 1919 he reported the first case of bilateral glioma of the retina in which the nonenucleated eye was treated with radium and recovered useful vision. The patient had been under observation for over ten years. In 1929, after visiting Gonin abroad, he performed the first Gonin operation for retinal detachment done in the United States at the Herman Knapp Memorial Eye Hospital. In 1934, through his efforts the first checking station for tonometers was established at the same hospital.

The third feature was his early grasp of anaphylaxis and his correct predictions of its possibilities. In 1914 he was awarded the Lucien Howe prize of the Medical Society of the State of New York for a contribution to the experimental study of anaphylaxis. He correctly evaluated Elschnig's work in the production of experimental anaphylaxis with tissues of the eye as antigens, and stated¹

The facts regarding the hypersensitization of the entire organism and of the eye by the use of extracts from uvea are bringing us nearer to one of the most vital questions in ophthalmology vis -sympathetic ophthalmia."

He also predicted¹ (page 27), "I should not consider [it] improbable that anaphylaxis may be some day a routine and a very valuable method of differential diagnosis."

Genius, like Egypt's monarch timely wise,
Erects its own memorial ere it dies

As long as society values progressive practical research, untiring enthusiasm in helping one's fellowman and constant striving for truth, Dr. Mark J. Schoenberg will be with us.

ISADORE GIVNER, M.D.

¹ Schoenberg, M. J. Contribution to Experimental Study of Ocular Anaphylaxis, *Ophthalmology* 11:4, 1914.

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Conjunctiva

MENINGOCOCCIC CONJUNCTIVITIS R D REID and L H BRONSTEIN, J A M A 124: 703 (March 11) 1944

A child of 2 years had purulent conjunctivitis of the right eye. A smear showed numerous intracellular and extracellular gram-negative diplococci. The condition of the eye grew worse. General examination revealed nothing of significance except for a temperature of 99.6 F. Cultures of material made by rubbing the fresh swab of exudate on the surface of a chocolate agar plate yielded an abundant growth of oxidase-positive, gram-negative diplococci. The organisms were agglutinated with antimentingococcus serum type I and failed to agglutinate with anti-meningococcus serum type II or III or with antigenococcus serum. With sulfathiazole therapy and irrigations of the eye with a solution of boric acid, there was no longer any purulent discharge on the third day, and the child was dismissed from the hospital.

The authors conclude that the diagnosis of meningococcic conjunctivitis should be suspected in cases in which gram-negative intracellular diplococci are seen in smears of pus and no obvious source of the infection is discernible.

W ZENTMAYER

UNILATERAL FOLLICULAR CONJUNCTIVITIS DUE TO MOLLUSCUM CONTAGIOSUM J A MAGNUS, Brit J Ophth 28: 245 (April) 1944

A woman aged 53 had acute catarrhal conjunctivitis with superficial keratitis of the right eye, which had developed after influenza. Examination of the nose, throat and sinuses revealed nothing abnormal. A culture was sterile. At the end of a month there was temporary improvement. A relapse occurred, and follicles developed in the conjunctiva. It was not until three months after the first examination that several umbilicated, small tumors were noticed on both lids. Two of these encroached on the lid margins. The tumors were removed, and the growths at the margin of the lid were destroyed by electrocautery. A piece of the conjunctiva was excised. The histologic examination confirmed the diagnosis of follicular conjunctivitis molluscum contagiosum.

The article is illustrated

W ZENTMAYER

Cornea and Sclera

FURTHER STUDIES ON RELATIONSHIP OF CORNEAL VASCULARIZATION TO RIBOFLAVIN DEFICIENCY J F MCCREARY, J V V NICHOLLS and F F TISDALE, Canadian M A J 51: 106 (Aug) 1944

McCreary and his associates report on studies to determine whether or not examination with the slit lamp and the photographic procedure give comparable data and to throw further light on the effect of riboflavin on corneal vascularization and symptoms of ocular fatigue. The results obtained from photographing the corneoscleral junction with the ophthalmic camera and the results of examination with a slit lamp are not significantly different. A study to demonstrate the effect of riboflavin on corneal vascularization was carried out, using both photography and examination with the slit lamp. The subjects studied were 41 students in the photographic division of the Canadian Air Force who had been provided with a ration containing when served 2.9 mg of riboflavin per day for a period of one year. Approximately one-half the subjects were given a supplement of 3.3 mg of riboflavin three times a day for two months, and the other half received placebos. There was no consistent change in corneal vascularization in either the treated subjects or the controls. The instillation of a simple irritant in the conjunctival sac caused collapsed, dysfunctional blood vessels in the cornea transitional zone and conjunctiva to become engorged. This study seems to show that a uniform vascularization of the periphery of the cornea is not a safe basis for a diagnosis of riboflavin deficiency existing at the time of examination. Such a lesion may be due to riboflavin deficiency, but the deficiency could have occurred at any time prior to the examinations. Also, these blood vessels could have been reactivated by some cause other than lack of riboflavin.

J A M A (W ZENTMAYER)

General

TREATMENT OF ASTHENOPIA—NONPATHOLOGIC AND NONREFRACTIVE IN ORIGIN R H PINO and G L HULTIN, Am J Ophth 27: 520 (May) 1944

Pino and Hultin give the data on 125 patients with asthenopia who were not relieved by glasses or other means. The ages ranged from 12 to 54. They feel that orthoptic training may be helpful.

in ways over and above the more definite procedures for which such exercises are more commonly used

W S REESE

General Diseases

CONGENITAL CATARACT AND OTHER ANOMALIES FOLLOWING GERMAN MEASLES IN THE MOTHER A B REESE, Am J Ophth 27: 483 (May) 1944

Reese reports 3 cases of congenital cataract and congenital heart lesions in infants whose mothers had contracted rubella within the first month of pregnancy. He refers to similar cases reported in Australia after a severe epidemic of rubella.

W S REESE

ALLERGIC REACTION OF TEARS OF TUBERCULOUS PATIENTS C GARBINO, Arch de oftal de Buenos Aires 18: 617 (Nov) 1943

Observations were made on children, including 20 healthy children, 22 with phlyctenular hypersensitive or nonallergic keratoconjunctivitis and 10 children with tuberculosis.

The tears were injected, using the Mantoux technic for inoculation with tuberculin. The observations were divided as follows: Tears of children with hyperegenic phlyctenular keratoconjunctivitis were inoculated into children with the same type of conjunctivitis, into children with the nonallergic phlyctenular type, into children with the allergic nonphlyctenular type and into healthy children.

The control tests consisted in injection of tears of healthy children into allergic children, with phlyctenular or nonphlyctenular conjunctivitis and into nonallergic children with phlyctenular and nonphlyctenular keratoconjunctivitis.

The results were 100 per cent positive in the first group, 100 per cent negative in the second group and 100 per cent negative in the control groups. The author states that these experiments tend to confirm the pathogenic concept of Weeks in regard to the cause of phlyctenular keratoconjunctivitis.

H F CARRASQUILLO

Injuries

ERRORS IN THE ROENTGENOGRAPHIC DIAGNOSIS OF FOREIGN BODIES IN THE EYE J A SENA, Arch de oftal de Buenos Aires 18: 622 (Nov) 1943

In the diagnosis of an intraocular foreign body one must consider the probable and the true evidence. The first is furnished by the history, the study of the wound and the reactive phenomena. The only true sign is the visualization of the foreign body inside the eye, and this, unfortunately, is possible in only 5 per cent of cases. For this reason the use of the roentgenogram is of the utmost importance in the diagnosis, although not

altogether infallible. Even with a negative roentgenogram, the existence of an intraocular foreign body cannot be absolutely excluded. The author has been able to show roentgenographically a steel particle weighing only 1.6 mg and a copper fragment weighing 0.97 mg.

The following rules should be observed for exactness of roentgenographic studies: the use of soft rays produced by a tube of fine focus, the avoidance as much as possible of osseous structures, and the proper immobilization of the head and eye to be examined, in order to make visible in the film the contour of the eyeball, or in some way to make possible an estimation of its contour.

Sená recommends the Sweet technic and the geometric method as the best procedure. The only objection to its use is the necessity for a special apparatus. Attention is called to the possible fallacy of the roentgenographic diagnosis as proved in observations in 3 cases of his own. In 1 case a defect in the roentgenologic technic indicated the presence of a foreign body, while the clinical investigation gave negative evidence; in the second case the roentgenogram did not show the foreign body, while the clinical examination demonstrated its presence, and in the third case the roentgenographic examination showed that the foreign body was extraocular, while the clinical findings indicated that it was intraocular.

H F CARRASQUILLO

Ocular Muscles

EXOPHTHALMIC OPHTHALMOPLEGIA I D FAGIN, R W PAGEL and H H SAND, Am J Ophth 27: 504 (May) 1944

The authors give the following summary:

"1. The clinical history and findings of postmortem examination of a patient with exophthalmic ophthalmoplegia are reported.

2. The syndrome of exophthalmic ophthalmoplegia is briefly reviewed."

W S REESE

DUTIES AND TRAINING OF AN ORTHOPTIC TECHNICIAN W B LANCASTER, Am J Ophth 27: 515 (May) 1944

Lancaster feels that training of orthoptic technicians has been deficient in psychology, the art of teaching, the laws of learning and the methods of habit formation of conditioned reflexes.

W S REESE

RECESSION OF THE TROCHLEA FOR REDUCING THE ACTION OF THE SUPERIOR OBLIQUE MUSCLE W L HUGHES, Am J Ophth 27: 1123 (Oct) 1944

Hughes reports 8 cases of recession of the trochlea for overaction of the superior oblique muscle. He states that the procedure is simple, effective and safe and can be done with local anesthesia.

W S REESE

DIVERGENCE EXCESS CONSIDERED AS AN ANOMALY OF THE POSTURAL TONUS OF THE MUSCULAR APPARATUS A POSNER, Am J Ophth 27: 1136 (Oct) 1944

Posner gives the following summary

"1 A case of divergence excess combined with an esophoria is reported

"2 The prevailing theories regarding the nature of divergence excess are discussed

"3 It is shown that divergence excess is due neither to excessive stimulation of the divergence center nor to an anomalous position of rest dependent on anatomic factors

"4 It is proposed to regard divergence excess as an anomaly of the postural tonus of the extrinsic muscular apparatus in an atavistic sense

"5 According to this view, the eyes are capable of maintaining one of two alternative postures a more primitive divergent one, or a more recently acquired parallel one, depending on the degree of cortical control which is being exercised"

W S REESE

Orbit, Eyeball and Accessory Sinuses

THE EXOPHTHALMOS OF HYPERTHYROIDISM J H MULVANY, Am J Ophth 27: 589 (June) 1944

This is part I of a long article on exophthalmos based on the Hunterian lecture delivered in February 1939. It deals with differentiation on the basis of the mechanism, pathologic picture, symptoms and treatment of two varieties of exophthalmos associated with hyperthyroidism

W S REESE

PROGRESSIVE EXOPHTHALMOS IN TOXIC DISEASE OF THYROID GLAND REVIEW OF RECENT LITERATURE, WITH REPORT OF CASE OF PROGRESSIVE POST-THYROIDECTOMY PROPTOSIS IN A SIX YEAR OLD NEGRO GIRL G M HAIK, Arch Surg 48: 214 (March) 1944

Haik states that treatment of exophthalmos associated with hyperthyroidism, particularly the variety which becomes progressive after thyroidectomy, has been unsatisfactory. Thyroidectomy frequently seems to aggravate it. Recent studies indicate that the cause of exophthalmos accompanying hyperthyroidism is local edema, sometimes associated with hypertrophy of the extraocular muscles. The author reports a case of progressive post-thyroidectomy exophthalmos which he observed in a Negro girl aged 6 years. The case is of interest because toxic thyroid disease in very young children is unusual, and is even more unusual in young Negro children. The character of this patient's toxicity was evidenced by her extreme nervousness, her voracious appetite, with continued loss of weight, her constantly elevated pulse rate, respiratory rate and temperature, the crises which developed on two occasions, and the degree of damage to the liver demonstrated ante mortem by serial tests of function and confirmed by postmortem examination. The child's parents disregarded instructions given them when she was dismissed after the first operation. Ten months later irreparable damage to the eyes had occurred. The optic tissues removed at Naffziger's unroofing operation showed edematous changes, which were also present, though to a lesser degree, in the tissues removed post mortem. The case seems to fit into the "special ophthalmic type" of goiter described by Means and his associates. It may be that the use of radiation, rather than thyroidectomy, might have saved the child's eyes and ultimately her life. It is reasoned that with a less abrupt alteration in the endocrine balance induced by irradiation there is a greater chance for more gradual readjustment of the optic structures.

J A M A (W ZENTMAYER)

The Pupil

A SIMPLE METHOD FOR THE EARLY DIAGNOSIS OF ABNORMALITIES OF THE PUPILLARY REACTION H J STEARNS, Brit J Ophth 28: 275 (June) 1944

The procedure suggested by Stern is to throw a pinpoint light on the eye with the slit lamp in such a way that it just enters the pupil near the margin of the iris, this causes a light reaction, and the pupil contracts. This means that the margin of the iris moves toward the center of the pupil and prevents the light pencil from entering the pupil. As no light now reaches the retina, the stimulus for the contraction of the pupil is no longer present, the pupil dilates and thus again allows the pencil of light to reach the retina. The whole mechanism starts anew. This artificial hippus continues regularly in the normal eye so long as the light pencil enters the pupil. Physiologic differences, such as age, color of the iris and errors of refraction, have no influence on the reaction. Elderly persons and persons with dark irises show less extensive movements, but in every normal person the reaction is easily produced. The pupil contracts and dilates ten times in seven to eight seconds.

In cases of such conditions as latent syphilis and early tabes, with clinically normal pupillary reactions, the artificial hippus could not be produced with the slit lamp. Usually a good, if not extensive, contraction followed the first stimulus, then either the pupil did not dilate sufficiently to let the light pencil enter the eye, or a few irregular, sluggish contractions followed after which the pupil finally remained immobile.

W ZENTMAYER

Physiologic Optics

A REPLY TO CERTAIN CRITICISMS OF ANISEIKONIA W B LANCASTER, Am J Ophth 26: 943 (Sept) 1943

Lancaster gives a brief presentation of the methods of measuring aniseikonia and of the principles involved and then considers the allegations and criticisms. A few cases are reported, with sufficient data that one may form one's own opinion

W ZENTMAYER

Retina and Optic Nerve

A CASE OF RUPTURE OF THE RETINAL CYST CAUSING RETINAL DETACHMENT C D SHAPLAND, Brit J Ophth 28: 236 (April) 1944

A soldier aged 28, seven weeks before examination of his eyes, had felt a sharp, shooting pain, lasting two or three minutes, in the region of the right temple and felt dizzy and faint

In the right eye a flat detachment of the retina involved the macula. At the 7 to 9 o'clock position there was a prominent, thin-walled cyst with a delimiting band of retinochoroidal pigment disturbance. The wall of the cyst had evidently ruptured just behind the ora serrata, leaving a ragged dialysis of the retina. A diathermy operation was successful in replacement of the retina. Visual acuity, which had been 3/60, improved to 6/24, and a wide reentering angle in the field flattened out.

The article is illustrated

W ZENTMAYER

Trachoma

TRACHOMA W G FORSTER and J R McGIBONY, Am J Ophth 27: 1107 (Oct) 1944

In a study of trachoma among the North American Indians, it was found that there was only a slight decrease in the incidence of the disease between 1912 and 1938, but following the introduction of the sulfonamide compounds, in 1939, there was a notable reduction in the incidence.

Pannus must be present if the diagnosis of trachoma is to be made.

Local therapy with sulfonamide compounds has not been encouraging.

Over 90 per cent of the patients were cured after one course of treatment if an adequate dose of sulfanilamide was employed.

Conditions not responding to sulfanilamide therapy are probably not trachomatous.

W S REESE

Tumors

LEIOMYOMA OF THE IRIS W T DAVIS, E SHEPPARD and W J ROMEJKO, Am J Ophth 27: 467 (May) 1944

The authors report a case of leiomyoma and suggest excision, rather than enucleation, of such

a tumor because it does not invade surrounding structures or the filtration angle

W S REESE

EXTRADURAL DIPLOIC EPIDERMOIDS PRODUCING UNILATERAL EXOPHTHALMOS E H THORNHILL and B ANDERSON, Am J Ophth 27: 477 (May) 1944

Thornhill and Anderson give the following summary and draw the following conclusions.

"Extradural diploic epidermoids producing unilateral exophthalmos are not usually considered among the possibilities in the differential diagnosis of the causes of this condition. None the less, the condition may exist in areas adjacent to the orbit and may be the cause of exophthalmos. The possibility that unilateral exophthalmos is due to such a lesion can probably be proved or eliminated by X-ray studies once the possibility is recognized by the typical scalloping of the edges with marginal increase in bone density demonstrated through proper angulation and exposure."

"Complete removal and a cure was obtained in this case through the supra-orbital approach. It is doubtful whether this particular type of tumor ever occurs so far back in the orbit (the tumor arises from diploic spaces which are not present in the walls of the orbit) as to justify the trans-frontal approach recommended by neurosurgeons."

W S REESE

EPITHELIAL TUMORS OF THE IRIS M K ASBURY, Am J Ophth 27: 1094 (Oct) 1944

Asbury discusses tumors of the iris and cites reported cases. From a detailed study of 4 cases she concludes that in spite of relatively benign histologic characteristics, these tumors all showed invasiveness and local destructiveness and were probably malignant in the same sense as is rodent ulcer of the skin (basal cell carcinoma).

W S REESE

Vision

SUPPRESSION AMBLYOPIA H S SUGAR, Am J Ophth 27: 469 (May) 1944

Sugar draws the following conclusions:

"1. In disagreement with Peter's statement that amblyopia in squinting eyes is a symptom of squint and not its cause, suggestive evidence has been presented indicating that suppression and amblyopia precede the development of certain nonparetic squints and follows the development of other nonparetic squints and those of paretic origin."

"2. Anisometropia is the predominating associated factor in nonsquinting amblyopic subjects, whereas high isohyperopia is the most frequent factor in cases of amblyopia with convergent squint."

"3 Nonparetic squint probably requires suppression plus another factor for its development This may be the accommodation-convergence relationship or simply the assumption of the dissociated position after suppression has been obtained in one eye The age factor is obviously of considerable additional importance

"4 Suppression amblyopia is a more accurate term than amblyopia ex anopsia, implying, as it does, an active rather than a passive process

"5 The conclusions drawn may be of aid in adding links to the chain of evidence as to the cause of squint Further clarification of the reason for normal muscle balance in a large number of amblyopic subjects, particularly a possible relationship to peripheral fusion, is necessary"

W S REESE

Therapeutics

THE USE OF TYROTHRICIN, A BACTERIAL EXTRACT, IN THE TREATMENT OF MARGINAL ULCERS OF THE CORNEA S BLOOMFIELD, Am J Ophth 27: 500 (May) 1944

Bloomfield reports 4 cases of resistant marginal ulcer in which tyrothricin was used, with gratifying results The drug may be readily applied to the conjunctival sac in effective concentrations It has been proved effective against gram-positive organisms

W S REESE

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

Pan-American Congress of Ophthalmology — The program for the coming meeting of the Pan-American Congress of Ophthalmology, which is to be held in Montevideo, Uruguay, during the week of Nov 25, 1945, is practically completed and will be published in the near future As was done at the last congress, all papers will be in Spanish, Portuguese or English, with projected translations as the paper is being presented

Any recognized ophthalmologist is eligible for membership The annual fee is \$5, payable to Dr Conrad Berens, treasurer, 218 Second Avenue, New York 3 That fee entitles the member to receive gratis the official organ of the congress — *Ophthalmologia Ibero Americana*, which is a quarterly trilingual abstract journal

Tentative travel arrangements are being made with the Pan-American Airways, as well as the American Express Company, but these cannot be concluded definitely until there has been a further turn in world affairs

Society of the Kellogg Fellows of the Pan-American Congress of Ophthalmology — The Society of the Kellogg Fellows of the Pan-American Congress of Ophthalmology was formed to help in bringing about a close relationship between the ophthalmologists of the Americas and to aid in raising the level of the theory, practice and teaching of ophthalmology in the Western Hemisphere The society met in October 1944, adopted the statutes of the organization and elected the following officers Harry S Gradle, MD, (United States), honorary president, Manoel da Silva, MD (Brazil), president, Olga Ferrer, MD (Cuba), secretary

The membership of the society is now composed of twenty-eight fellows from the following eighteen countries Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Paraguay, Peru, Puerto Rico and Venezuela

Address — Olga Ferrer, secretary, Institute of Ophthalmology of the Presbyterian Hospital, 635 West One Hundred and Sixty-Fifth Street, New York

William Thornwall Davis Postgraduate Course in Ocular Surgery, Pathology, Ocular Motility and Orthoptics — The eighth annual William Thornwall Davis Postgraduate Course will be given at the George Washington University School of Medicine, Washington, D C, May 28-June 2, 1945 The Army Institute of Pathology, directed by Col J E Ash, Medical Corps, United States Army, will give the course in ocular pathology, as he has done in former years The courses in ocular surgery, ocular motility and orthoptics will be given by members of the resident staff of the department of ophthalmology, under the direction of Dr Ernest Sheppard, professor of ophthalmology The course is limited to 30 registrants

SOCIETY NEWS

Cancellation of Annual Meeting of Association for Research in Ophthalmology — The Association for Research in Ophthalmology has canceled its 1945 meeting in cooperation with the war travel and convention program Essayists are requested to reserve their manuscripts for a possible meeting in 1946, in conjunction with the annual sessions of the American Medical Association

UNIVERSITY NEWS

Appointment for Dr Ernest Sheppard — Dr Ernest Sheppard has recently been appointed as professor of ophthalmology of the George Washington University School of Medicine, to succeed the late Dr William Thornwall Davis This appointment was directed by the board of trustees of the university on Dec 1, 1944

Society Transactions

EDITED BY DR W L BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H JOHNSON, M D, *Chairman*

WENDELL L HUGHES, M D, *Secretary*

Regular Meeting, Jan 15, 1945

Pigmented Meningioma and Neuroepithelioma of the Optic Nerve. Report of a Case DR CHARLES A PERERA

An interpretation of this extraordinary case is difficult. The orbital tumor was distinct from the neuroepithelioma and appeared to arise in the sheath of the optic nerve. The hyalinized masses may represent massive hyalinization of capillaries. The presence of chromatophores in meningiomas has been reported, and the cells are known to occur in neurofibromatosis. Gliomas of the optic nerve stimulate glial proliferation and practically never recur after removal of the main tumor. Perhaps the neuroepithelioma in this case produced a chemical agent which passed forward into the sheath of the optic nerve and stimulated growth of the pigmented meningioma.

Trauma and Ocular Lesions. A Study in Reciprocal Relations DR PERCY FRIDENBERG

Millions are engaged in activities involving violent physical exertion in industry and even in "heavy" sports, in which serious injury to the limbs and the viscera, the skull and the bones, is almost an everyday occurrence. Detachment of the retina as a result of such exertion is practically unknown. Direct injury, especially to an eye predisposed by high myopia and its attendant pathologic changes, is, on the other hand, a probable factor in the causation of retinal detachment.

DISCUSSION

DR ARNOLD KNAPP Dr Fridenberg has brought out many interesting and suggestive points. As far as retinal detachment is concerned, I think that trauma is an insignificant etiologic factor. Of the 400 cases of retinal detachment in which I made careful examinations, there was direct trauma in 32 and indirect trauma in 20. In the latter group the defense mechanism of which Dr Fridenberg speaks is the only explanation that is, the eyes were predisposed to the development of a detachment.

DR MORRIS DAVIDSON Dr Fridenberg has dealt with the subject in a comprehensive manner, but there is one thing in particular to which I

should like to refer. First, the importance of the relation of trauma to lesions of the eye is not realized. Perhaps some figures may be of interest. Of every 1,000 persons with injury examined at the Department of Labor, 250 present a problem in causal relations, and 125, a problem of the kind that Dr Fridenberg discussed, namely, optic nerve atrophy, retinal detachment, interstitial keratitis, glaucoma and similar conditions. This problem will be a more important one in the future because of a greater number of workmen's compensation cases to be dealt with after the war. There is another important aspect with which some may not be familiar. A new amendment was passed at the last session of the New York state legislature which changes the emphasis of the topic that Dr Fridenberg discussed. As you know, in the past the insurance carrier paid for the loss of an injured eye regardless of a preexisting defect. Now, in order to create more jobs by stimulating employers to take on defective persons and war veterans, the New York state law says that this loss will be apportioned between two parties. The insurance company will pay a part of the compensation allowed, and from a special fund to be created by the state the rest will be paid. The insurance company will pay for the loss resulting from trauma, and the state fund will be used to pay for the predisposition factor, so the emphasis on the causal relation will be less. The insurance company will be concerned less with the causal relation and more with finding out how much of the whole compensation it is to pay. The problem of the physician will be to appear on the witness stand and state, for example, whether the trauma accounts for 20 per cent of the loss and predisposition for 80 per cent, or whether the trauma accounts for 30 per cent of the loss and predisposition for 70 per cent. The problem will be to weigh the importance of the two roles, which is as difficult as the aspect dealt with by Dr Fridenberg.

DR PERCY FRIDENBERG I want to mention a point I passed over when I was discussing the defense mechanism. This mechanism concerns not only the eye but the whole body, and the factors which bring about the defense of the eye will also produce tension of the abdominal muscles, forced exhalations and all the accompaniments of heavy work. A number of cases were mentioned in which detachment of the retina was noted after coughing, sneezing or vomiting. Authors state that such actions could not cause

detachment, but they are accompanied with exactly the same reflexes in the defense mechanism of the eye. The grip on the globe is to protect it from sudden opening, like the protection provided by a pressure bandage. The lid has been called the protective dressing of the eye, and it might also be called its guardian angel.

Value of Cultures Before Operations for Cataract DR JOHN H DUNNINGTON and DR D LOCATCHER-KHORAZO

This article will be published in a later issue of the ARCHIVES

Relative Effects of Thiouracil, Iodine and Subtotal Thyroidectomy on the Exophthalmos of Hyperthyroidism DR M NOEL STOW, Baltimore

This study, of which the present paper is a preliminary report, is summarized as follows:

The comparative effects of thiouracil on a series of 10 patients, of iodine on 12 patients and of subtotal thyroidectomy on 10 patients, all with established hyperthyroidism, were studied.

The data obtained in this investigation were tabulated with special reference to the ophthalmopathy of exophthalmos and the associated widening of the palpebral fissures.

An attempt was made to correlate the normal with the abnormal hormonal activity of the thyroid and the sequential established pathologic states with reference to their possible alteration, especially in their ocular manifestations, by means of the therapeutic adjuncts of thiouracil, iodine and subtotal thyroidectomy.

Although the total number of cases available for study was not large enough to constitute a true biostatistical sampling, it appears (*a*) that the administration of thiouracil not only does not effect improvement in the exophthalmos of hyperthyroidism but tends to permit the exophthalmos to progress unchecked or to accelerate it or both, (*b*) that the preoperative administration of iodine in cases of recent onset tends either to effect no change in the exophthalmos or to bring about some improvement in it, and (*c*) that subtotal thyroidectomy most frequently results in progression of or no change in the proptosis.

The exophthalmos of hyperthyroidism continues to present a most difficult therapeutic problem. The administration of iodine is effective in some cases, but they must be carefully selected. The more radical procedure of subtotal thyroidectomy is frequently indicated when medical treatment is ineffective. Thiouracil, on the contrary, is most useful in alleviating the general symptoms, unfortunately, it may prove to be without benefit with regard to the ocular manifestations of hyperthyroidism. It is urged, therefore, that whether or not ocular symptoms are present, repeated complete and careful ophthalmologic examinations be done routinely on

all patients with hyperthyroidism to whom thiouracil is administered.

DISCUSSION

DR DAVID P BARR There seems to be no question that Dr Stow has demonstrated an increase in the protrusion of the eyeballs in a number of cases following treatment with thiouracil and that this change is comparable in extent to the increase which is observed in some cases after subtotal thyroidectomy. Especially interesting is his demonstration that the protrusion of the eyeballs in some cases may be slightly diminished by the administration of iodine. These observations are substantiated in part by the recent unpublished observations of Dr B M Dobyns, at the Mayo Clinic. Dr Dobyns has permitted me to mention them. He studied 223 patients treated by subtotal thyroidectomy, making approximately 10,000 separate measurements of exophthalmos in the postoperative period. He was able to show in almost all his patients an increase in the prominence of the eyes following thyroidectomy. He was unable to show that iodine increased exophthalmos. Like Dr Stow, he found that the exophthalmos became greater after the use of thiouracil. In 1 case he demonstrated an increase in protrusion of 4 mm following the use of this drug.

My associates and I at New York Hospital have been interested in the use of thiouracil for about sixteen months, and during that time we have used the drug in the treatment of 85 patients. Sixty of them have been treated long enough to permit one to judge the full therapeutic effect. Some of them have received thiouracil continuously for nine months and most of them for six months or longer. Early in our studies we heard from Dr R H Williams, of Boston, that malignant exophthalmos, similar to the form not infrequently observed after thyroidectomy, had developed in a patient treated with thiouracil. We therefore were prepared to believe that we might produce serious protrusion of the eyeballs with this active drug. Consequently, we made careful measurements with the Hertel exophthalmometer before and at intervals after the use of the drug. I am sure that the accuracy of our measurements is not comparable to that of Dr Stow's, for they were carried out by a number of persons. We did, however, observe increases as high as 3 mm in 1 patient and as high as 2 mm in several others. No patient exhibited a diminution in the protrusion of the eyeballs. We did not measure the width of the palpebral fissure. We did, however, observe that many of the patients treated with thiouracil had diminished lid spasm and lid lag, so that, while the actual protrusion was not ameliorated, exophthalmos appeared to be lessened. We treated 3 patients who would be regarded, I think, as having malignant exophthalmos. In none of them was there a

measurable increase in the degree of protrusion. In 2 patients there was no improvement in function or in clinical symptoms. In the third patient the degree of lid spasm had diminished so much that all troublesome symptoms disappeared.

Of course it is impossible to generalize from such scant evidence, but it is our impression at present that thiouracil does not lessen the protrusion of the eyeballs, that in some cases it increases it but that in such cases the increase is so slight that one cannot regard it as dangerous to the eyes, even in cases in which there are beginning symptoms of malignant exophthalmos.

DR G K SMELSER (by invitation). It is difficult for me, whose experience with exophthalmos lies entirely in experimental work with guinea pigs, to follow Dr Stow's paper and Dr Bari's discussion. Dr Stow's paper is particularly timely because, as you know, thiouracil is a new drug which is being used widely, and not only at Cornell, the New York Hospital and the Presbyterian Hospital. Many patients are being treated by medical men who are less experienced in the examination of eyes than are ophthalmologists, and they sometimes are surprised that the ocular symptoms are not improved. It is interesting that this report confirms the extra-thyroid origin of exophthalmos. At one time it was thought that exophthalmos was one of the characteristics of hyperthyroidism and that the secretion of the thyroid was responsible for the exophthalmos. I think that belief is no longer held. Apparently, one must look to some gland or structure outside the thyroid for the cause of the protrusion of the globe and of the other symptoms of exophthalmos, which go hand in hand with those referable to the thyroid and are the result of the same malfunction or have the same etiologic factor. Apparently, on the basis of laboratory experiments which my associates and I have carried out, the pituitary does seem to be involved. The observations of Dr Stow tend to show that something outside the thyroid is responsible for the protrusion, for he has demonstrated that with the shift toward normal of the serum cholesterol, the body weight and the metabolism, all the symptoms have been abolished or alleviated except the exophthalmos.

Several questions come to my mind. First, Dr Stow reported that in some of the thiouracil-treated patients there was no change in the exophthalmos, or the eye protruded even more, but that the spasm of the lid or the width of the palpebral fissure did not change. What is the controlling factor in the lid spasm and the width of the palpebral fissure? I shall go back to my guinea pigs, for it seems that the palpebral fissure may be controlled by two mechanisms. In rodents with hyperthyroidism the palpebral fissure is controlled largely by the sympathetic fibers. The hyperthyroidism could, I think, be cured with thiouracil, for the basal metabolic rate decreases

and the toxic manifestations are lessened. They should also decrease with the use of iodine. However, in a number of experiments the width of the palpebral fissure did not decrease, even though involvement of the sympathetic fibers was ruled out. The lid lag was due to a forward movement of the globe. I do not know whether this could be the cause of the widened palpebral fissure in the patients with subtotal thyroidectomy.

I think Dr Stow's observation as to the effect of iodine is an original contribution. In a review of the literature, one finds almost anything; one author says the drug is of benefit and another that it is not, and one cannot make up one's mind whether iodine in the form of compound solution of iodine U S P is of value in the treatment of exophthalmos. When, in our experiments with guinea pigs, we produce exophthalmos with pituitary extract, we can give the animals any quantity of iodides without a decrease in the exophthalmos. Apparently, from these experiments one would judge that the iodine molecule does not interfere with the action of the pituitary extract when injected parenterally. Then (this is a working hypothesis), if this is the case, and the iodine given the patients in Dr Stow's series had a beneficial effect on the exophthalmos, it must have been due to a release of pituitary hormone from the pituitary gland itself, it being always assumed that the pituitary is the basic cause of the exophthalmos.

Another suggestion might be made. A number of years ago Moran, in an interesting paper read at Atlantic City, N. J., suggested that part of the exophthalmos of hyperthyroidism was really sympathetic in origin and was due to the palpebral muscle pulling back on the orbital septum and thus exerting pressure on the retrobulbar tissues, which pushed the globe forward. On this basis, the correction, or the decrease in exophthalmos, which Dr Stow found associated with hyperthyroidism, might be due to the relaxation of the sympathetic stimulus.

The mechanism of the effect of iodine and of thiouracil on the exophthalmos is, I think, one of the most interesting and important phases of the work on exophthalmos. Certainly, the problem is a great one. The help that is to be obtained is now almost entirely in the clinical field, and a good example of this has been given by Dr Stow.

DR ISADORE GIVNER. I should like to make two observations. After listening to this paper, one may feel that the process of exophthalmos is probably not a reversible one, since thiouracil, iodine in most cases, and thyroidectomy produce no reduction in the exophthalmos. I should like to cite a case which will leave one a little more optimistic. A woman who had been operated on for exophthalmic goiter noticed an increase in the exophthalmos following thyroidectomy. This amount became stationary. The patient subse-

quently became pregnant, and the question came up as to whether the pregnancy should be allowed to go on to term. It was decided to let it go through without interruption. After she had been pregnant four months, the exophthalmos began to show improvement and continued to do so up to the time the baby was born. Measurements showed that the exophthalmos had receded 4 mm., demonstrating the fact that the changes in muscle which are responsible for exophthalmos are reversible. Interestingly, the baby was born with exophthalmos, which persisted until the child was 3 months old. The child is now 3 years old, and the mother's exophthalmos has stayed at the lower level. This brings up the question as to what happened during pregnancy that unfavorably influenced the exophthalmos. Did the baby's thyroid or thymus act for the mother, or were there certain hormonal changes which occurred either at the placental barrier or in the mother which produced changes in the muscles of the eyes? I am not in a position to answer these questions, but they suggest material for investigative work.

Dr Otto Lowenstein and I studied 22 cases of exophthalmic goiter by pupillography, and in 21 of these there was a characteristic pupillographic curve, namely, a redilation block, which was interpreted as indicating a central sympathetic lesion, probably in the hypothalamus. This fits in well with the theoretic discussion presented this evening and gives tangible evidence of central disturbance.

DR M NOEL STOW: I wish to thank Dr Barr and Dr Smelser for discussing the paper. I have nothing to add to their discussion. In answer to Dr Smelser's question as to the cause of the widened palpebral fissure in hyperthyroidism, the theory that is most plausible to me is that of sympathetic stimulation; this hypothesis is based on the accepted theory that in hyperthyroidism the threshold of the sympathetic nervous system is lowered. I think this holds true in the early stage of exophthalmos, but there is more than

mere stimulation of the sympathetic system, particularly when the condition is of some duration. In fact, it seems to me that when the hyperthyroidism is reduced, whether by thiouracil, iodine or operation there will no longer be pronounced sympathetic stimulation, but if the process has gone on long enough, the eyes become so proptosed that it is as much a mechanical as a sympathetic mechanism, or even more. In every case in which there was widening of the palpebral fissures there was a measurable exophthalmos. I am unable to answer the question of Dr Givner with reference to the patient who had a decrease in her proptosis during pregnancy. I know that similar cases have been reported in the literature, but I am unable to explain the exact mechanism.

I do not wish to leave the impression that thiouracil is not a valuable drug. I believe that it is one of the better drugs and that in the future it may be found to be the best one, but I believe that when it is given in cases of exophthalmos the eyes should be followed very closely. In this series, which was small, there was no case of malignant exophthalmos and none of corneal involvement, and there was only moderate conjunctival chemosis in the worst cases. The protrusion was pronounced in only 1 case, in others the changes were slight. However, one should follow the ophthalmologic signs in the patients treated with thiouracil thoroughly enough and long enough to know more about the effect of the drug. Dr Lahey believes that the best combination for preoperative preparation is thiouracil and iodine. It has been found that in a patient who has been prepared for operation with thiouracil there is an increased vascularity of the thyroid gland and that bleeding at the time of operation is most troublesome, but Lahey has given a verbal statement to another physician, who gave it to me, that in his hands administration of thiouracil for about three weeks, then discontinuance of the drug for one week, followed by administration of iodine is the most satisfactory preparation for operation he has thus far found.

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All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6^e, France

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Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping
Place Peiping Union Medical College, Peiping Time Last Friday of each month

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

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Place Birmingham and Midland Eye Hospital

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Secretary Dr D Williams, 193 Macquarie St, Sydney

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Secretary Dr H D Dastur, Dadar, Bombay 14, India
Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

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Place Edinburgh and Glasgow, in rotation

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April to November All correspondence should be
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In compliance with the request of the Office of Defense
Transportation and in the interest of the national war
effort a meeting will not be held in 1945

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Place 91 Lincoln Park South, Newark Time 8 45
p m, second Monday of each month, October to May

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third Saturday of each month, October to May, in-
clusive

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Place Good Samaritan Hospital, Portland Time
Third Tuesday of each month

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Secretary-Treasurer Dr Linley C Happ, 124 Water-
man St, Providence
Place Rhode Island Medical Society, Library, Prov-
idence Time 8 30 p m, second Thursday in
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Place University Club, Salt Lake City Time 7 00
p m, third Monday of each month

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Time First Monday in January, March, May and
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Atlanta, Ga

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Secretary Dr Thomas R O'Rourk, 104 W Madison
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Secretary Dr Luther E Wilson, 919 Woodward Bldg,
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Place Tutwiler Hotel Time 6 30 p m, second
Tuesday of each month, September to May, inclusive

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President Dr Michael J Buonaguro, 589 Lorimer St,
Brooklyn

Secretary-Treasurer Dr Benjamin C Rosenthal, 140
New York Ave, Brooklyn 16

Place Kings County Medical Society Bldg, 1313 Bed-
ford Ave Time Third Thursday in February, April,
May, October and December

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President Dr Walter F King, 519 Delaware Ave,
Buffalo

Secretary-Treasurer Dr Sheldon B Freeman, 196
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Time Second Thursday of each month

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of each month from September to May

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St, Chicago 2

Secretary Dr W A Mann, 30 N Michigan Ave,
Chicago 2

Place Continental Hotel, 505 N Michigan Ave

Time Third Monday of each month from October
to May

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STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati

Secretary Dr A A Levin, 441 Vine St, Cincinnati

Place Cincinnati General Hospital Time 7 45 p m,
third Friday of each month except June, July and
August

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Chairman Dr Shandor Monson, 1621 Euclid Ave,
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Secretary Dr Carl Ellenberger, 14805 Detroit Ave,
Cleveland

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Chairman Dr W S Reese, 1901 Walnut St,
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Clerk Dr George F J Kelly, 37 S 20th St,
Philadelphia

Time Third Thursday of every month from October
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Columbus, Ohio

Secretary-Treasurer Dr T Rees Williams, 380 E
Town St, Columbus 15, Ohio

Place University Club Time 6 15 p m, first Mon-
day of each month, from October to May, inclusive

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THROAT SOCIETY

Chairman Dr C B Collins, 704 Medical Professional
Bldg, Corpus Christi, Texas

Secretary Dr L W O Janssen, 710 Medical Profes-
sional Bldg, Corpus Christi, Texas

Time 6 30 p m, third Tuesday of each month from
October to May

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OTO-LARYNGOLOGY

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Dallas 1, Texas

Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,
Texas

Place Dallas Athletic Club Time 6 30 p m, first
Tuesday of each month from October to June The
November, January and March meetings are devoted
to clinical work

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 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa
 Time 7 45 p m, third Monday of every month from September to May

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 Secretary Dr Cecil W Lepard, 1025 David Whitney Bldg, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time First Wednesday of each month, November to April, inclusive

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Raymond S Gou, 545 David Whitney Bldg, Detroit 26
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

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 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany
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President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas
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 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

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 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

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 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

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 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

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 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2
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 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio
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 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada
 Time Second Thursday of October, December, February and April

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 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn
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NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

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 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans
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 Secretary Dr Wendell L Hughes, 131 Fulton Ave, Hempstead, N Y
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 Secretary Dr Benjamin Esterman, 983 Park Ave, New York
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President Dr James P Luton, 117 N Broadway, Oklahoma City
 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City
 Place University Hospital Time Second Tuesday of each month from September to May

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 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
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President DR Thomas Sanfacon, 340 Park Ave, Paterson, N J
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J
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 Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia
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 Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh
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 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va
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 Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis
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 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center
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 Secretary Dr Clarence A Veasey Jr, 421 W Riverside Ave, Spokane, Wash
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 Secretary-Treasurer Dr Richard W Wilkinson, 1408 L St N W, Washington, D C
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Chairman Each member in turn
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 Place Office of chairman Time Last Tuesday of each month from October to May

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INHERITED CATARACT IN THE B GENEALOGY

OCCURRENCE OF DIVERSE TYPES OF CATARACT IN THE DESCENDANTS OF ONE PERSON

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ROCHESTER, NY

The numerous publications on developmental cataract, as summarized by Nettleship,¹ Harman-Groenouw,² Clausen³ and Waardenburg⁴ have tended to show a uniformity in the type of cataract observed within any family line. Nevertheless it is sometimes found that certain of the cataractous persons in a given pedigree have a type of opacity of the lens significantly different from that presented by the remaining affected members of the family (Kries,⁵ Gjeising 1878 quoted from Harman,² Nettleship,¹ Harman⁶ Groenouw,² Halbertsma⁷ Walsh and Wegman¹⁰). This fact has been commented on by various observers, and a question raised from time to time as to the etiologic relationships of the various types. The present paper will de-

From the Departments of Surgery and Medicine, the University of Rochester School of Medicine and Dentistry, and the Strong Memorial and Rochester Municipal Hospitals

1 Nettleship, E. On Heredity in the Various Forms of Cataract, *Roy London Ophth Hosp Rep* **16** 179, 1905, **16** 389, 1906.

2 Harman, N B. Congenital Cataract, in *Treasury of Human Inheritance*, edited by K Pearson, London, Cambridge University Press, 1912, vol 1, p 126.

3 Groenouw, A. Beziehungen der Allgemeinleiden und Organerkrankungen zu Veränderungen und Krankheiten des Sehorgans, in Gräfe, A. and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, ed 3, Leipzig, W Engelmann, 1920.

4 Clausen, W. *Vererbungslehre und Augenheilkunde*, Zentralbl f d ges Ophth **11** 209 1924.

5 Waardenburg, P J. *Das menschliche Auge und seine Erbanlagen*, The Hague, Martinus Nijhoff, 1932.

6 Kries, M. Ueber den Spindel-Staer und die Accommodation bei demselben, *Arch f Ophth* **23** 211, 1877.

7 (a) Nettleship, E., and Ogilvie, M. A Peculiar Form of Hereditary Congenital Cataract, *Tr Ophth Soc U Kingdom* **26** 191, 1906 (b) Nettleship, E. Lamellar Cataract, "Coppock" or Discoid Cataract, and Retinitis Pigmentosa, Affecting Different Members of the Same Pedigree, *ibid* **28** 226, 1908.

8 Harman, N B. Congenital Cataract. A Pedigree of Five Generations, *Tr Ophth Soc U Kingdom* **29** 101, 1909.

9 Halbertsma, K T A. Ueber familiare juvenile Katarakt, *Klin Monatsbl f Augenh* **80** 108, 1928.

10 Walsh, F B., and Wegman, M E. Pedigree of Hereditary Cataract, Illustrating Sex-Limited Type, *Bull Johns Hopkins Hosp* **61** 125, 1937.

scribe a genealogy of 123 people, 44 with cataract, which is remarkable for the variety of forms the cataract assumes and will discuss the question of the genetic relationship of the various types of cataract seen in this and comparable pedigrees.

THE B FAMILY

The persons comprising this genealogy are the descendants of one William B (I 1) who in 1849, at the age of 24, migrated from Chelmsford, Essex County, England, to Ontario Center in the northwestern part of the state of New York, when this region was first settled. He was known to have cataracts, and with his poor vision was able to do only farm and outdoor labor. He could never see well enough to read and in his later years his vision became progressively worse until he was unable to get around outside of his house. He died at the age of 74 of cancer. W B was believed to have inherited the cataracts from his mother. Nothing further back is known of the family, except that there were other members who remained in England who were also afflicted with cataracts. No other members of this family are known to have migrated to America. Two of B's daughters (II 6 and II 10), who are still living supplied the foregoing information and contributed greatly to the construction of the pedigree (fig 1).

The first members of the family whom we saw were IV 46 and IV 47, when they came to the Eye Clinic of the Strong Memorial and Rochester Municipal Hospitals. IV 13 was seen next, and the various members of his line of the family were then checked. This was followed by an examination of II 10 and her descendants. Other members of the family were examined as the opportunity presented itself. Additional information was gathered about the family from almost all of those seen. Most of the members of the family have remained in the same section of the country, living within a few miles of each other, and a fairly close family contact has been maintained, so that it is well known within the family which members have cataract, except for

the youngest generation Confirmation of the presence of cataract was usually made by more than one person in those cases in which we were unable to make an examination Newborn infants in the family were watched carefully by the parents and the relatives for the first evidence of visual difficulty, and those having cataract were known from early childhood to have subnormal vision In no member of the family who was unaffected with cataract in childhood was cataract known to develop later in life

The majority of the family, whose industry is average, have remained in rural districts engaged in work such as that required of laborers, farmers and unskilled workmen A few have been factory workers No one in the family either with or without cataract has achieved unusual prominence or success in any field of work, nor were any persons encountered of the economically dependent and shiftless type The homes that were visited were average for their economic level Evidences of physical, moral or mental degeneracy in the family were absent Two persons, III 15 and IV 28, were said to be of subnormal mentality However, all whom we examined were of good physique and skeletal structure, with no evidence of rickets, and of apparently average intelligence Some of the children, both with and without cataract, were of unusually attractive appearance The teeth of nearly all the cataractous persons examined were inspected, there were no greater than average incidence of caries, and no malformations Only one person, IV 47, had a few horizontal ridges on his teeth No history of convulsions during infancy was elicited from any member of the family

Most of those with cataract whom we saw had had only one eye treated surgically, and with this eye possessed approximately normal corrected vision In a majority of the cases the surgical treatment up to about the age of 30 had been repeated discussions The cataract was unaccompanied by any other structural abnormalities of the eye A complicated myopia occurring in III 18 and some of her descendants required thin cataract lenses to correct the eyes after operation III 18 had a satisfactory intracapsular lens extraction, but high myopic degeneration caused poor vision IV 13, who also had extensive myopic retinal degeneration, had had bilateral extracapsular lens extractions followed later by retinal separations This type of myopia did not occur in the other lines with the cataract In only one instance (V 5) had surgical treatment consisting of discussion of one eye been followed by complications which were disastrous to vision

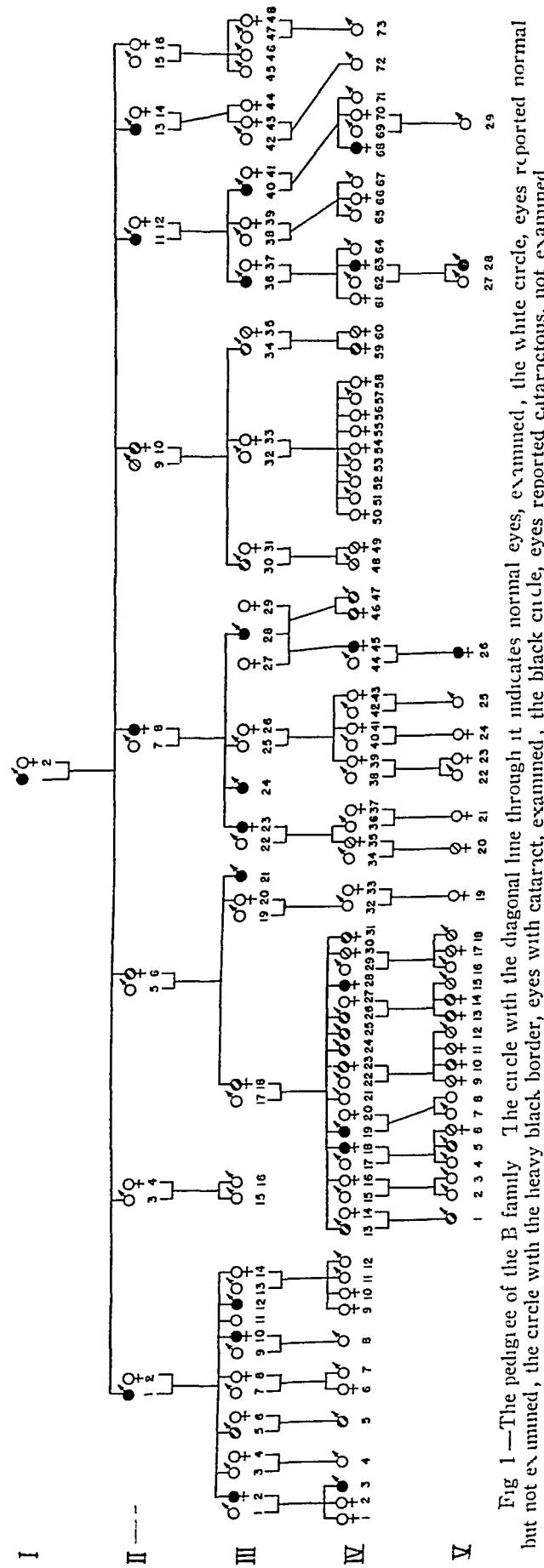


Fig 1.—The pedigree of the B family. The circle with the diagonal line through it indicates normal eyes, examined, the white circle, eyes reported normal but not examined, the circle with the heavy black border, eyes with cataract, examined, the black circle, eyes reported cataractous, not examined.

A detailed description of the B genealogy follows

II 1 D B had cataracts His vision had always been poor He was never able to read newsprint even between his fingers His vision gradually became worse,

anterior layers of the peripheral third of the lens were radiating opacities and vacuoles

II 11 C B had cataracts His vision had always been poor, but he was able to see better at night than in bright sunlight Both cataracts were removed at about the age of 65 He died at the age of 80

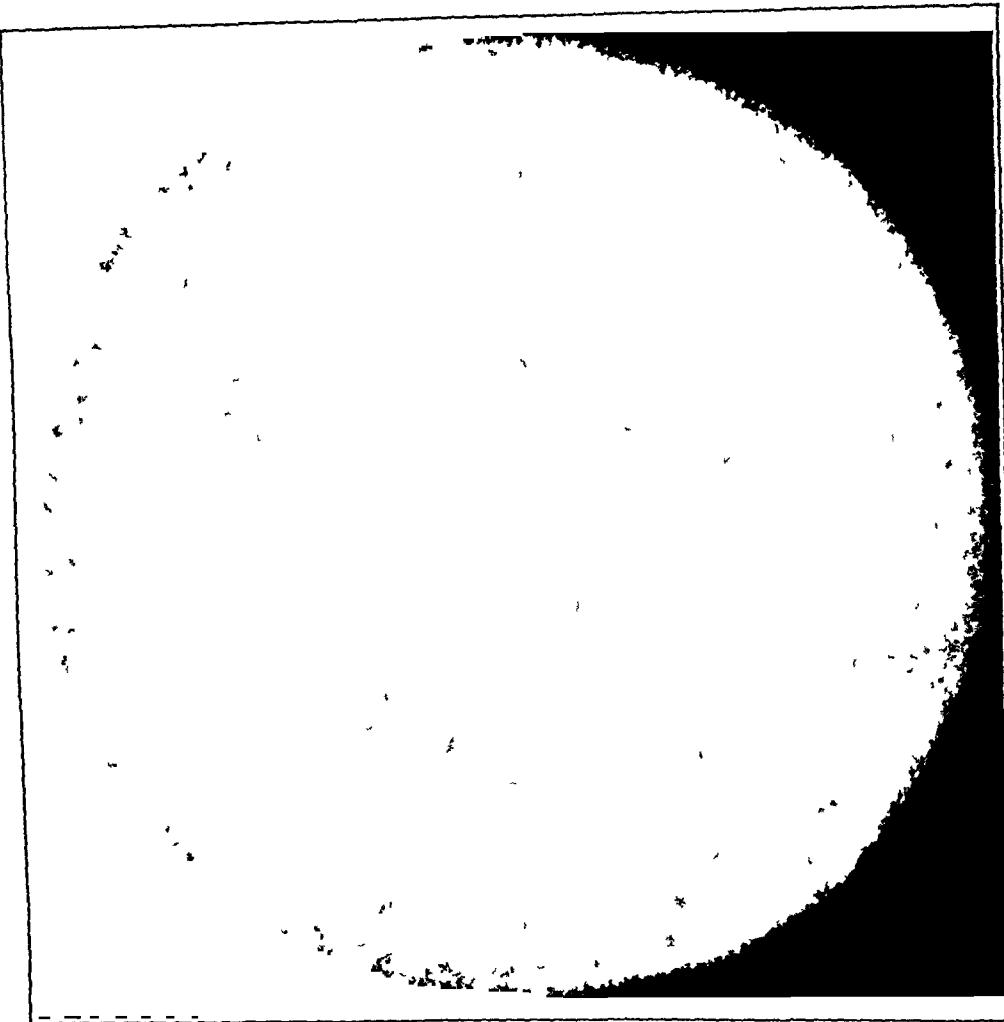


Fig 2—Ophthalmoscopic view of the cataract in II 6 (E B B, aged 82)

so that one cataract was removed at the age of 60 He died at the age of 74 years

II 3 G B had good vision throughout his life, and never wore glasses He died at the age of 74 years of heart disease

II 6 (fig 2) E B B, aged 82, had cataracts As a child at school she had difficulty with her vision, which during later years gradually became worse The cataract in the right eye was removed at the age of 60 with good corrected vision following Ophthalmoscopic examination of the left eye showed a complete white lens opacity

II 8 S B C had cataracts She had poor vision throughout life, becoming worse with age Operation was not performed She died at the age of 77 after prolonged heart trouble

II 9 Ophthalmoscopic examination was performed The lenses were clear

II 10 (fig 3) R B D, aged 74, had cataracts She had always had difficulty reading and was able only to read newsprint between her fingers with her hand shading her eyes, or when in a dark corner of a room She was never able to see well in a bright light On ophthalmoscopic examination through pupils dilated to 8 mm, a ring was seen encircling the middle half of the lens In the axial region were radiating, linear opacities, mixed with flakes and vacuoles, the latter being more common in the anterior layers In the

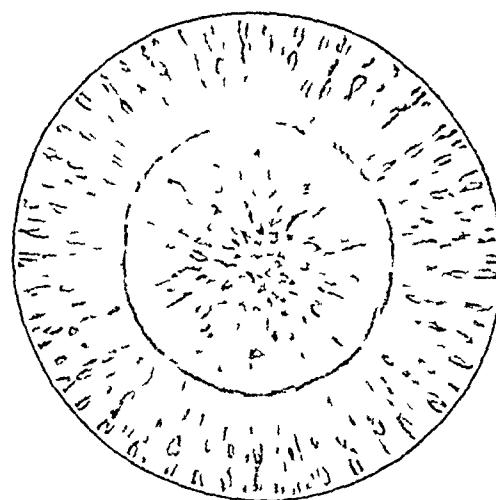


Fig 3—Ophthalmoscopic view of the cataract in II 10 (R B D, aged 74)

II 13 W B had cataracts He had poor vision throughout his life, and was forced to do outdoor work He died at the age of 55 of a sudden heart attack

II 16 M B R had good vision and could sew and read newsprint Death occurred at the age of 69

III 2 G B McF, aged 41, had cataracts One eye was operated on

III 3 C B had good eyesight Death occurred at the age of 20 from accidental scalding

III 5 D B Jr, aged 35, had cataracts Both cataracts were needed

III 8 G B V, aged 32, had good eyesight

III 10 E B M, aged 51, had cataracts

III 11 This child died at 3 years of age

III 12 L B had cataracts He had extremely poor eyesight He died at 35 years of age of tuberculosis

III 21 M B, aged 56, a storekeeper, had cataracts One eye was operated on at the age of 36 Vision in that eye with glasses was good

III 23 J C M, aged 70, had cataracts All her life she was forced to hold things very close She scolded and read with difficulty One eye had been operated on, the resulting vision was unknown

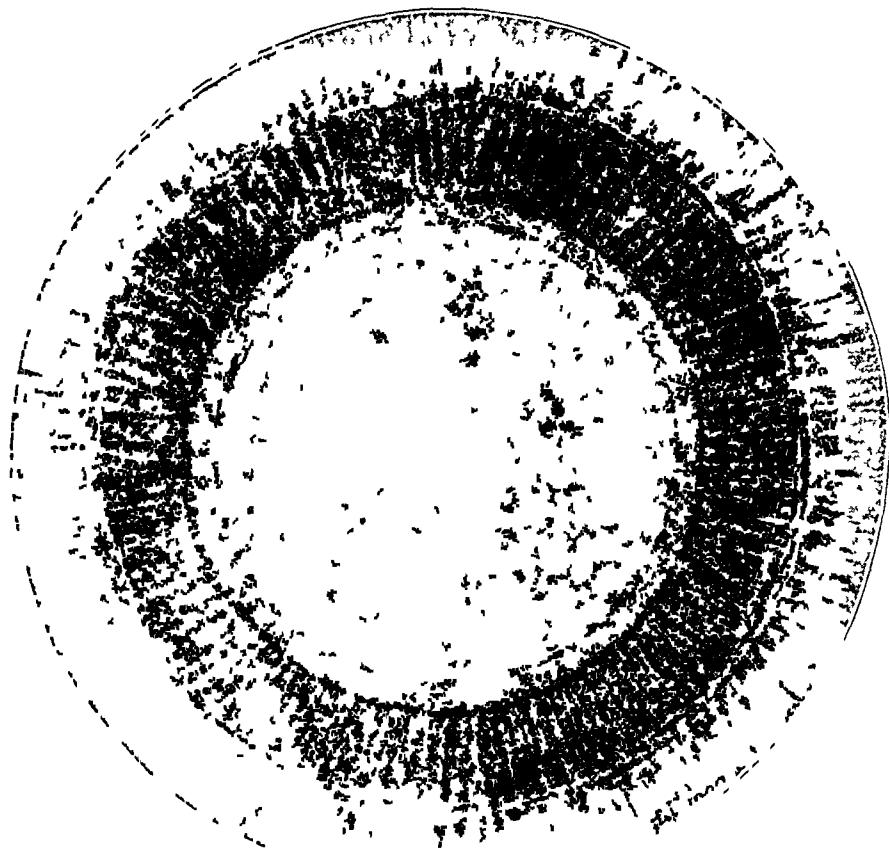


Fig 4—Slit lamp view of the cataract in III 18 (M B H, aged 61)

III 14 C B B, aged 44, had good eyesight

III 15 Eyesight was good He was described as feeble-minded Death occurred at the age of 48

III 16 A B, aged 50, had good eyesight

III 18 (fig 4) M B H, aged 61, had cataracts Vision had always been impaired She was unable to go far in school because of her eyesight In 1938, intracapsular cataract extraction with iridectomy was performed on her right eye Retinoscopic examination revealed vision in the right eye with a +6.50 D sph +2.50 D cyl to be 13/200 The media of this eye were clear There was a myopic conus with retinal degeneration, extending 4 disk diameters temporal to the disk On the lower and temporal peripheries were areas of retinal degeneration Vision of the left eye equaled hand movements Through the dilated pupil there was a dull red reflex around a central sphere, which was diffusely opaque, and in which were large whitish bodies scattered through all depths Each of these bodies was a uniformly white spherical opacity with slightly blurred borders Surrounding the large sphere was a thin zone of fine punctate opacities and farther out a linear zone In the peripheral outer fourth in the deeper layers of the anterior cortex was a fringe of radiating opaque spokes The posterior layers of the lens contained radial opacities

III 20 M B B, aged 51, had no difficulty with vision

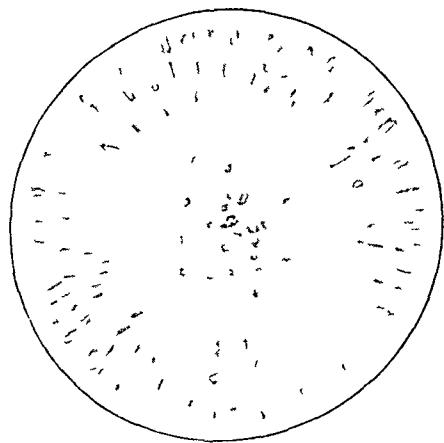


Fig 5—Ophthalmoscopic view of the cataract in III 30 (R D, aged 48)

III 24 B C, aged 61, had cataracts He always had extremely poor vision and stumbled over things until one eye was operated on, at about the age of 36

III 25 A C, aged 60, had good vision

III 28 W C had cataracts He preferred a dim light, in which he could read larger newsprint type, he was unable to read in bright sunlight He died at the age of 52 of a sudden attack of heart disease

III 30 (fig 5) R D, aged 48, had cataracts. He always had some difficulty in reading. His vision had gradually become poorer. An ophthalmoscopic examination through pupils dilated to 8 mm revealed around the middle third of the axis of the lens, and located more in the anterior layers, scattered, fine opacities together with numerous larger round ones which appeared as vacuoles. In the outer third of the lens were radiating clefts and vacuoles. The extreme periphery of the lenses was clear. The fundi were normal.

III 33 E D F, aged 41, had no visual difficulty.

III 34 (fig 6) G D, aged 36, had cataracts. He reads Ishihara color perception charts readily. Paredrine hydrobromide¹¹-homatropine hydrobromide was used as a cycloplegic for refraction.

Vision with a +175 D cyl, ax 70 in the right eye was 6/10-2, in the left eye with a +175 D cyl ax 85 it was 6/10-1.

In the deeper zones of the lens in the axial region were many powdery, much finer clumps of crystals, of brilliantly reflecting colors. In addition there were occasional small flakes. A few fine granular opacities were in the posterior zones. The fundi were normal.

III 35 Paredrine hydrobromide-homatropine hydrobromide was used as a cycloplegic for the refraction.

Vision in the right eye with a -175 D sph -100 D cyl, ax 55 was 6/5-3, in the left eye with a -175 D sph -075 D cyl, ax 80 it was 6/5-4.

Media, disks and macula were normal.

III 36 F B, aged 69 years, had cataracts.

III 39 M B S, aged 60 years, had good eyesight.

III 40 W B had cataracts. Death occurred at 62 from cancer.

III 43 E B T, aged 48 had good vision.

III 44 H B D, aged 45, had good vision.

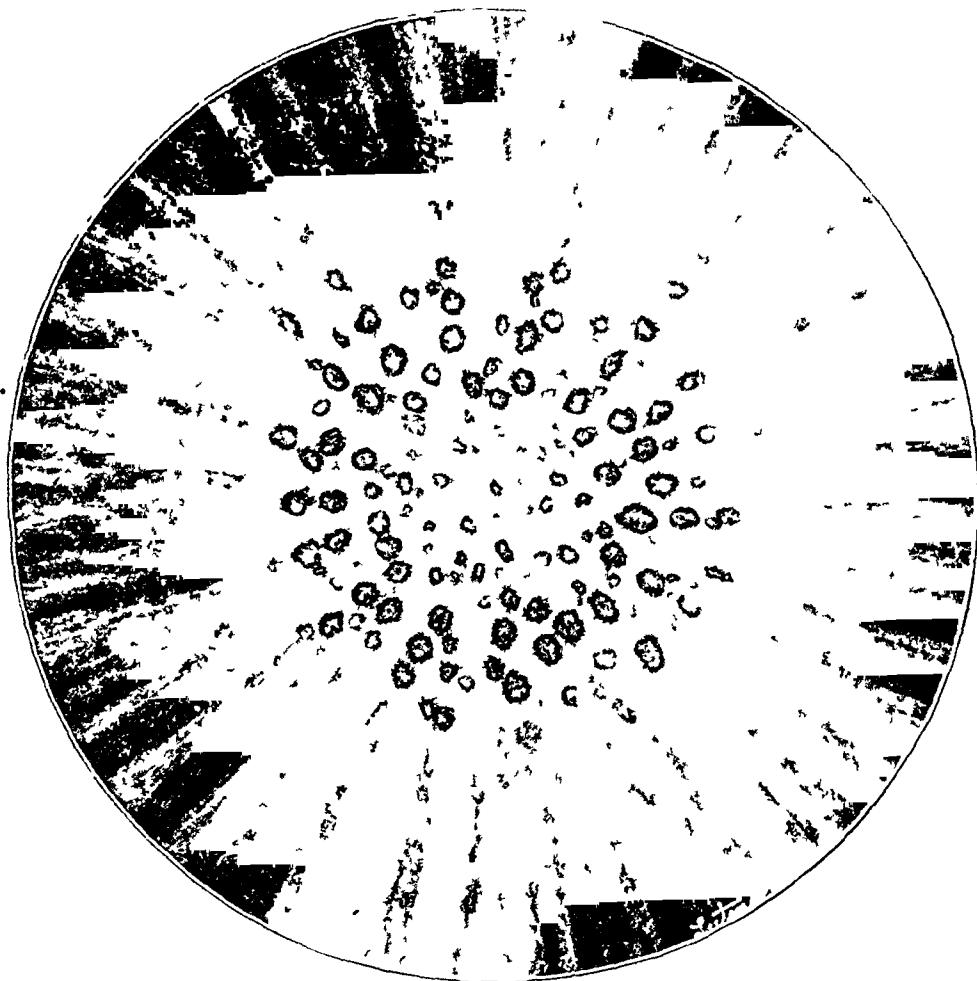


Fig 6—Slit lamp view of cataract in III 34 (G D, aged 36)

By retinoscopic examination, opacities were seen on the axial half of the lens without a sharply limited zonular distribution. With the slit lamp the opacities were seen to be larger and less numerous than those in his daughter IV 59 (fig 11), and were located in the anterior subcortex and in the anterior adult nuclear region. In the periphery of the deep anterior cortex there was a radial ring composed of spear-shaped opacities and clefts.

By direct illumination, the individual opacities resembled flakes of mica, the central portion of each was nearly clear, with its outer ring extremely iridescent.

¹¹ The composition of paredrine hydrobromide is parahydroxy- α -methylphenylethylamine hydrobromide, 1 per cent, made isotonic with sodium chloride and preserved with merthiolate, 1:100,000.

III 45 M R had good vision. Death occurred at 61 from cancer.

III 46 C R, aged 62, had good eyesight.

III 48 P R S, aged 60, had good vision.

IV 1, M McF, aged 17, and IV 2, B McF, aged 13, both had good eyesight.

IV 3 G McF, aged 10, had cataracts and eyesight was poor.

IV 4 G B, aged 21, in the army, had good eyesight.

IV 5 This member of the family, aged 5, had cataracts. Both lenses had been needled once.

IV 6, S V, aged 11, and IV 7, aged 6, had good eyesight.

IV 8 L M, aged 26, did not have cataracts.

IV 9, aged 24, IV 10, G B, aged 21, IV 11, F B, aged 19, in the army, and IV 12, W B, aged 8, all had good eyesight.

IV 13 E H, aged 43, had cataracts. Both cataracts were removed with iridectomies. Retinal separation in the right eye occurred in 1936. For a retinal separation in the left eye in 1943, operation was performed with perforating scleral diathermy, with successful restoration of reading vision. Although the fundi could not

at school. The cataract in the left eye was needled four times when he was 17 years of age. The left pupil was clear. Numerous vitreous opacities were seen. A 0.5 disk diameter white conus was seen below the left disk. The fundus was normal. Vision in the left eye with a +6.00 D sph \approx +1.50 cyl, at 60 was

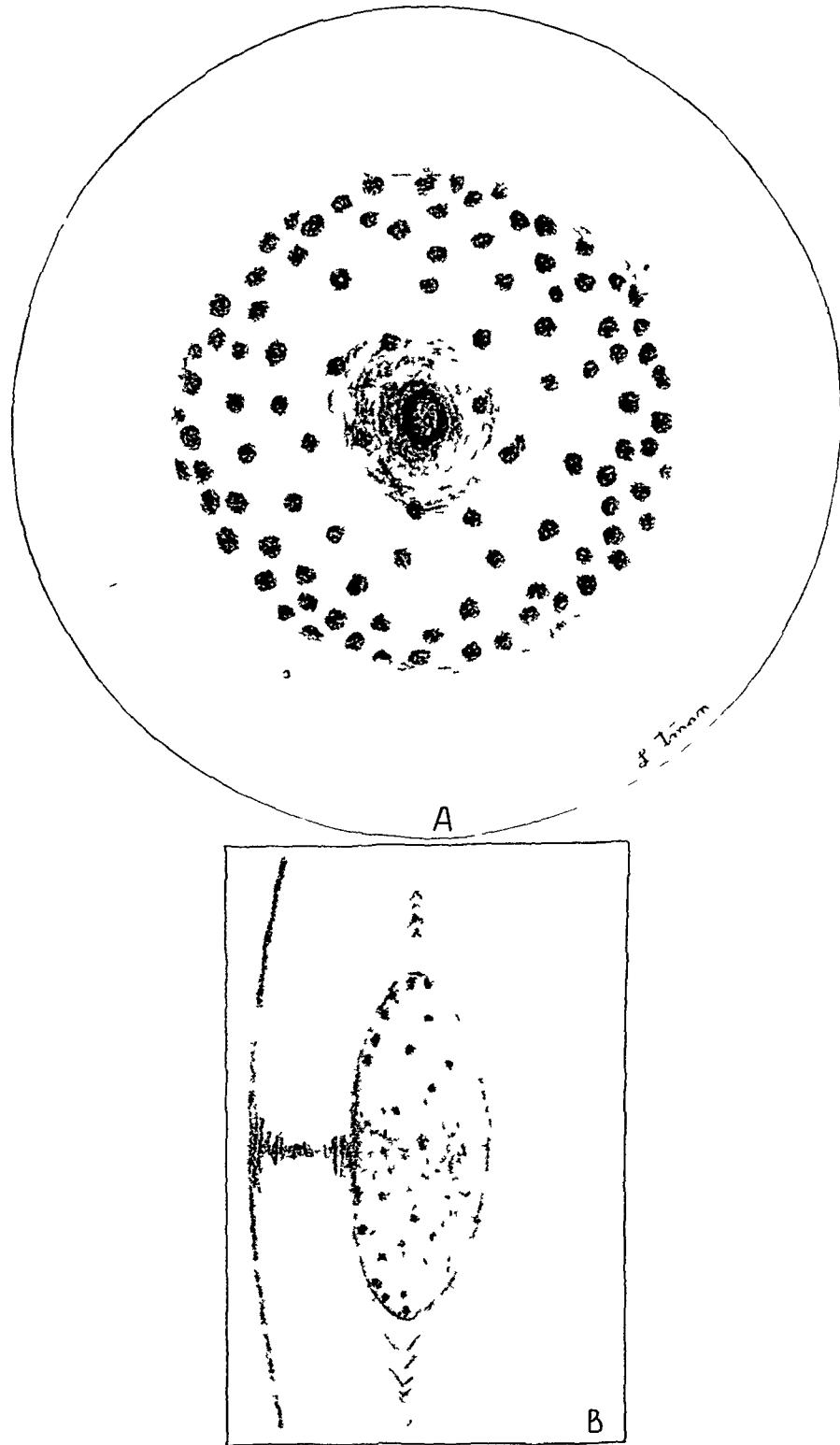


Fig 7—*A*, slit lamp view of the cataract in IV 18 (O H R aged 41); *B*, schematic cross section of the lens in the same person.

be seen clearly, extensive myopic degeneration was visible.

IV 16 G H J, aged 41 had no trouble with vision.

IV 18 (fig 7) O H R aged 41 had cataracts. He worked as a factory inspector. He had great difficulty

6/7.5, +3.00 D sph was added to read Jaeger's test type 2 at 36 cm. Vision in the right eye was limited to hand movements. The central half of the lens was visible through a dilated pupil as a slightly irregular spherical opacity with a narrow zone of very fine white

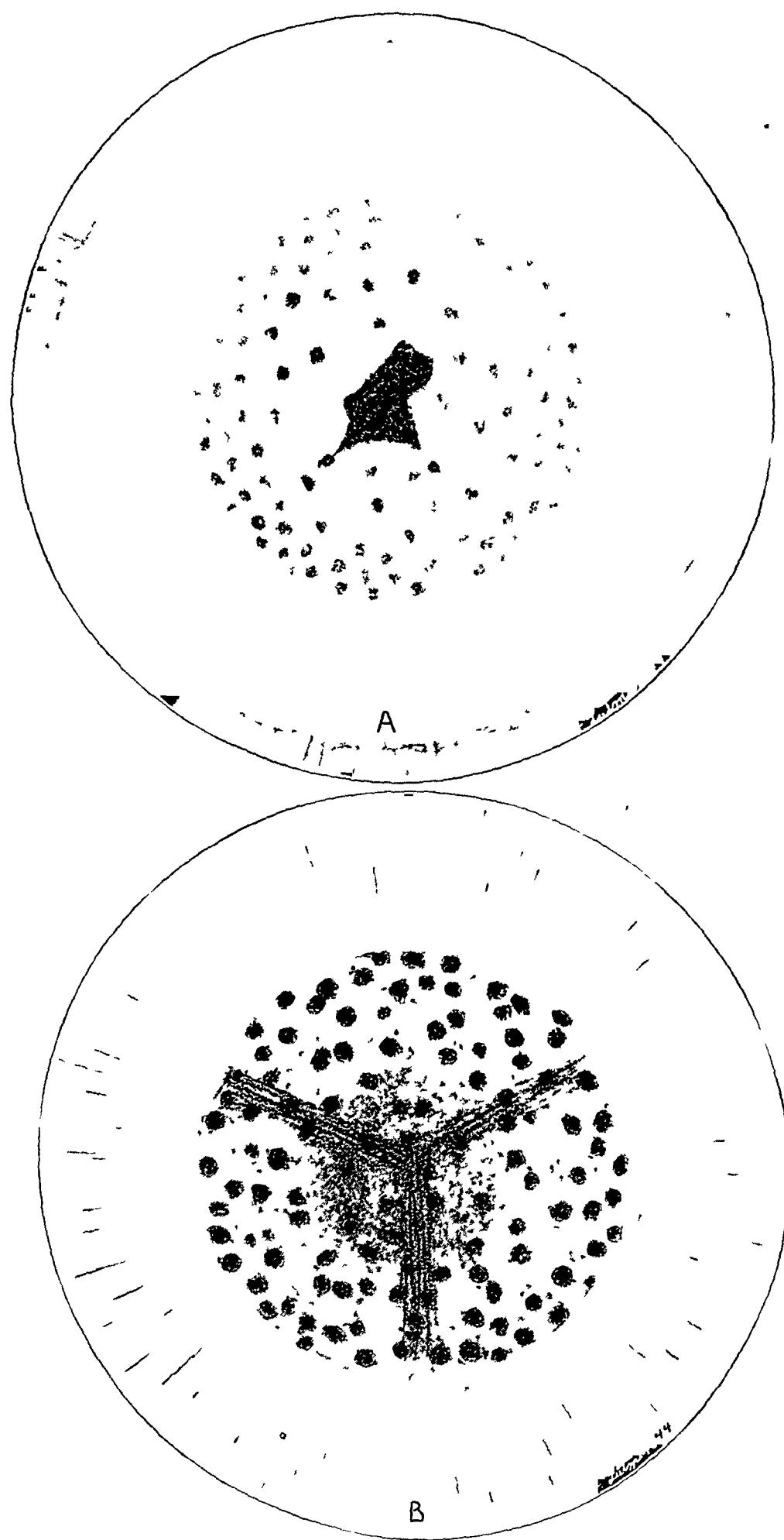


Fig 8.—A, slit lamp view of the cataract in IV 23 (M H D, aged 33) B, slit lamp view of the cataract in IV 24 (A H, aged 34)

specks surrounding it. The central nuclear opacity had flakelike opacities scattered throughout, more densely in the periphery, together with many finer punctate ones. These larger flakes possessed some thickness and a uniform opaqueness. An oval anterior polar opacity continued backward along the lens axis as a fusiform opacity to the nucleus. Opaque spokes were visible at different depths peripheral to the fetal nucleus, forming zonular riders.

IV 19 M H, aged 37, had cataracts. One eye was believed to have been operated on.

IV 21 S H, aged 35, had good vision with the aid of glasses.

IV 23 (fig 8 A) M H D, aged 33, had cataracts. The right eye was needled at the age of 16. Vision in this eye with correction was 6/6, in the left eye it was 2/200. Through the dilated left pupil the central half of the lens was a sharply outlined semiopaque sphere with opaque flakes at all depths, a greater number toward the periphery of this area. The individual flakes were uniformly dull opacities with slightly blunted margins, and were scattered through all depths of the nucleus, though less numerous in the deeper layers. The central two thirds of this nucleus was a dull opaque region rather clearly demarcated. A faint ring of powdery white spots sharply outlined the fetal nucleus. A thin line circled a more peripheral zone. Close to the periphery of the lens was a ring of slightly yellowish flakes, extending from the periphery in the anterior part of the cortex and limited to a narrow zone were radial, linear opacities which passed toward the center. At the anterior pole of the lens was a triangular iridescent white opacity with an opacity continuing backward to the nucleus.

IV 24 (fig 8 B) A H, aged 34, had cataracts. He worked as a factory packer. He attributed his inability to go further than eighth grade in school to his poor eyesight. The cataract in his right eye was needled three times at the age of 21. The left eye was divergent 15 degrees. Vision in the right eye with a +1300 D sph \odot +200 cyl, ax 20 was 6/6. The right disk showed slight physiologic cupping. The retina and macula were normal. Vision in the left eye was 3/200. With a retinoscope, through the dilated left pupil, the central half of the lens was seen to be occupied by a sharply delineated opacity without a red reflex, a red reflex existed peripheral to this. With the slit lamp the opaque, anterior Y suture of the fetal nucleus was clearly visible on the anterior surface of this central opaque sphere. The three arms formed notches at the periphery of the nucleus, each notch marked by an indentation of the thin zone of fine white opacities immediately surrounding the nucleus. Solid, grayish, oval and spherical bodies, somewhat denser toward the peripheral zone, were scattered through the anterior part of the fetal nucleus when examined by section. The central portion of the lens was a milky opaque zone. Peripheral to the fetal nucleus were fine white lines which, when followed individually through the different depths, were anterior and posterior fibers joining in an acute angle toward the periphery to form riders.

IV 25 R H, aged 33, had cataracts. He worked as an elevator operator. The cataract in the right eye was needled when he was 20 years old. He had always had poor vision, and completed the eighth grade at school with difficulty. Exotropia of 12 degrees was present in the left eye. Vision in the right eye with a +950 D sph was -6/7.5-1. Slight physiologic cupping of the optic disk was seen. The retina was normal. Vision in the left eye was 2/200. The central half of the lens was an opaque sphere surrounded by a narrow

zone of very fine dots, which in turn was surrounded by a second narrow peripheral zone that was faintly opaque. In the fetal nucleus were solid, white, round and oval bodies scattered at all depths, more of them anteriorly, where the spheres were arranged somewhat radially. Others were toward the periphery of the nucleus. An anterior fusiform opacity continued from the fetal nucleus to the anterior capsule of the lens where, at the anterior lens pole, there was a small shining capsular opacity. Peripheral to the fetal nucleus were linear, radiating white riders.

IV 26 (fig 9) M H, aged 30, had cataracts. He worked as a farmer. The left eye had been needled several times in the past year. An opacity still remained in the pupillary region. Vision in the right eye was 6/20-1. Through a dilated right pupil a red reflex was present which was broken up by numerous opacities radiating from the densest portion along the axis of the lens. Slit lamp examination showed a feather-like arrangement of opaque lens fibers along the sutures of the adult nucleus. Three small capsular and subcapsular opacities existed at the anterior pole. In the lower temporal periphery there was a single group of radiating opacities in the cortex. In the posterior subcortical and nuclear regions were similar opaque lens fibers along the sutures. In the cross section there was a zone deeper in the adult nucleus composed of very fine opaque strands. More centrally was a zone of faint minute specks, surrounding a central hazy opacity, in the center of which was an irregular dense white opacity. There were no flakelike opacities visible in the lens.

IV 28 D H, aged 28, had cataracts. This person was seen but not examined. She was of subnormal mentality.

IV 30 E H C, aged 26, had clear lenses as revealed by examination with a retinoscope through dilated pupils. With the slit lamp, approximately fifteen fine flakelike opacities were seen in the right eye posterior to the anterior Y suture, and on the left lens, in a similar position, about ten.

IV 31 B H, aged 23, had cataracts. The cataract in the right eye had been needled, and vision in this eye was 6/6 with a lens. Through the dilated left pupil an opacity of the fetal nucleus was observed with a narrow zone of fine powdery opacities surrounding it. In the fetal nucleus were scattered flakes, with a greater number toward the periphery, each flake a grayish opacity with a white center. Peripheral to the fetal nucleus were radiating anterior and posterior opaque fibers forming riders, and near the extreme periphery a ring of large white flat flakes.

IV 32 V B, aged 30, had good vision.

IV 35 B C D, aged 40, had good vision with glasses. Slit lamp examination of the lenses showed only an occasional punctate opacity, no more than average.

IV 36 E M, aged 38, had good vision. He wore no glasses.

IV 39 H C, aged 35, IV 41, F C, aged 33, and IV 43, M C, aged 30, all had good eyesight.

IV 45 B C S, aged 36, had cataracts. The left lens had been needled, with a good result. The family described the right eye as having a very noticeable white opacity in the pupil.

IV 46 D C, aged 16, had cataracts. In 1937, a sketch of her lenses as recorded on her chart showed a nuclear opacity such as occurred in most of the descendants of III 18. Refraction, with homatropine hydrobromide used as a cycloplegic, showed vision in the right eye with a -0.75 sph \odot -1.50 cyl, ax 180

to be 6/20 + 1, in the left eye, with -0.50 sph ⊖ -1.25 cyl, ax 170, 6/15 + 2. The cataract in the right eye was needled twice in 1937, that in the left eye twice in 1938. In 1940, an alternating exotropia developed. Refraction in 1943 showed vision in the right eye with +1.00 sph ⊖ +1.50 cyl, ax 94 to be 6/6.2, in the

IV 47 (fig. 10) R C., aged 12, had cataracts. The left lens was needled twice in 1940. The right lens was needled in 1941, and again in 1943 for a wrinkled posterior capsule. As first needling in each eye had been done before the patient came under our observation the type of cataract is unknown. In three clusters

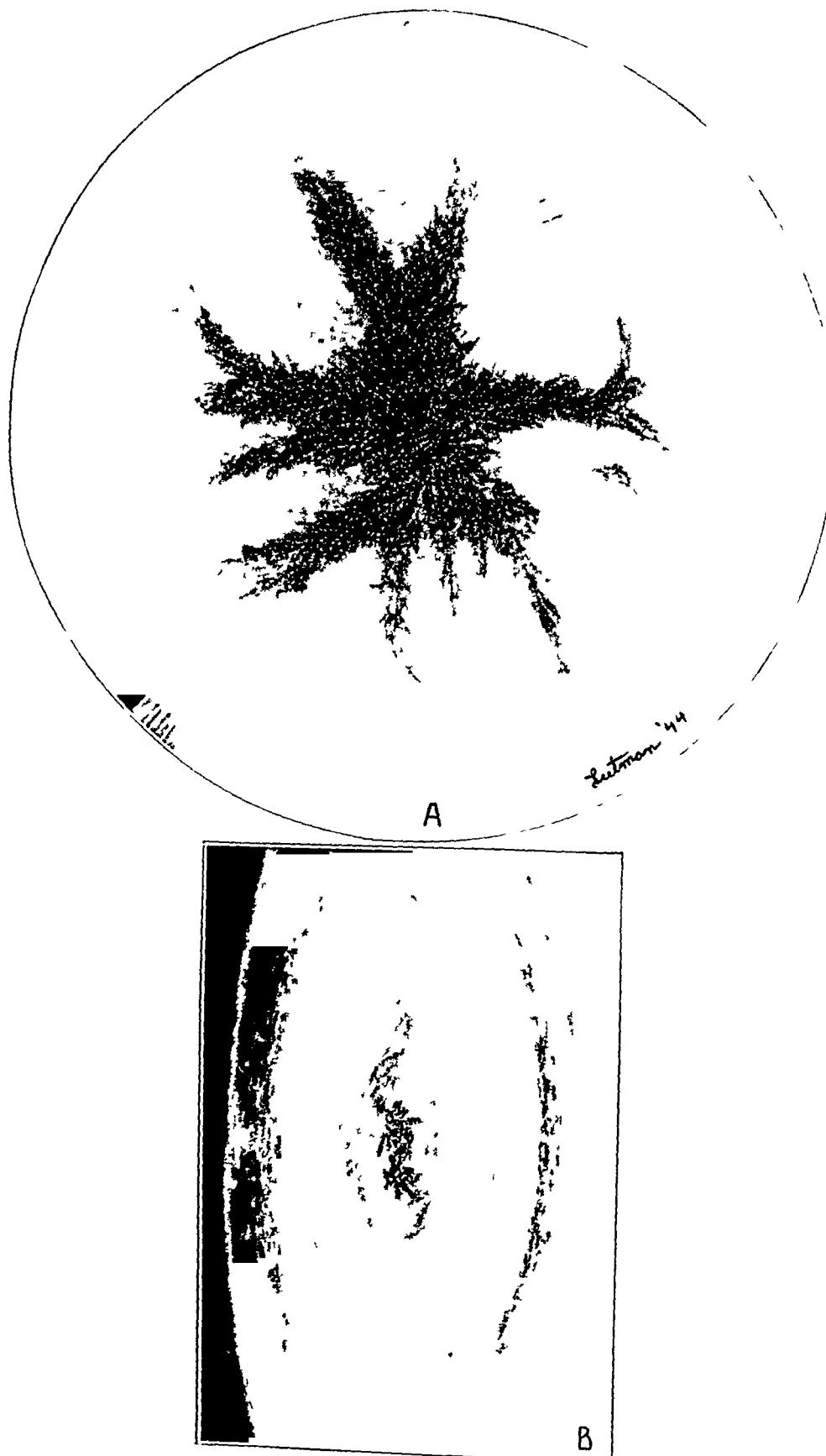


Fig. 9—*A*, slit lamp view of the cataract in IV 26 (M H, aged 30). *B*, schematic cross section of the lens in the same person.

left eye with a +1.00 sph ⊖ +1.25 cyl, ax 90, 6/5. There was a 15 degree right exotropia. On the right after-cataract were three small, spheroid white bodies similar to those found in IV 47 (fig. 10). The fundi were normal. Ishihara charts were rapidly read

on the posterior surface of the right cornea were 26 translucent, grayish, egglike globules an estimated 0.1 to 0.2 mm in diameter. An additional 33 of these bodies were scattered over the lower nasal iris. Several of the bodies were found in the lower left iris. Vision in the

right eye with a + 12.75 D sph \odot + 1.00 D cyl, ax 90 was 6/7.5 + 2, in the left eye with + 12.50 D sph \odot + 1.75 D cyl, ax 90, 6/7.5 - 2

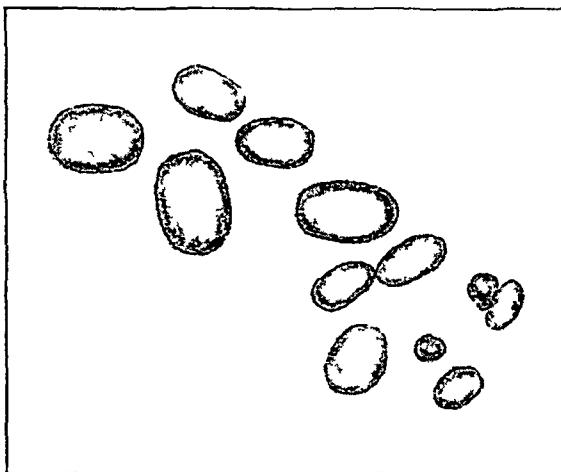


Fig 10—A group of the globules seen on the iris of the right eye of IV 47 (R C, aged 12), three years after discussion of the cataract

IV 48, aged 12, and IV 49, aged 4, were examined ophthalmoscopically, and the media were found to be clear

IV 50, aged 22, IV 51, aged 21, IV 52, aged 18, IV 53, aged 16, IV 54, aged 12, IV 55, aged 9, IV 56 aged 5, IV 57, aged 2, and IV 58, a baby, all had good eyesight

IV 59 (fig 11) B D, aged 16, had cataracts Her vision was gradually becoming slightly worse Refraction, with paredrine hydrobromide-homatropine hydrobromide used as a cycloplegic, showed vision in the right eye with a + 0.50 D sph \odot - 2.00 D cyl, ax 140 to be 6/7.5-2, in the left eye with + 1.00 D sph \odot - 2.25 D cyl, ax 60, 6/7.5 - 3 On retinoscopic examination no zonular opacities were seen, but along the middle half of the lens axis, somewhat radially distributed, were vacuoles and fine granular opacities Slit lamp examination of the lenses revealed that the individual opacities were smaller than those of her father, III 34, but of the same character Located in the anterior adult nuclear layer were scattered flakes, the periphery of each iridescent and each center almost clear Away from the axial region, the opacities were much less dense and appeared as vacuoles Deeper in this zone the opacities were groups of fine, shiny crystals located at all depths and without zonular distribution A more dense group of these opacities was located at the position of the posterior Y suture A few opacities were scattered throughout the center of the lens Scarcely any opacities were present in the more posterior zones of the lens The fundi were normal

IV 60 K D, aged 8, had refraction performed with atropine used as a cycloplegic Vision in the right eye with a + 0.25 D sph \odot + 1.00 D cyl, ax 90 was 6/10 in the left eye with a + 0.25 D sph \odot + 1.00 D cyl ax 75, 6/10 On retinoscopy the outline of the fetal nucleus was visible, but no opacifications were present By slit lamp, the lenses were clear, except for a few very fine granules in the center of the lens The fundi were normal

IV 61 E B, aged 40, had normal vision

IV 63 M B M, aged 38, had cataracts

IV 64 was believed to have good vision

IV 65 R S, aged 28, IV 66, and IV 67, aged 24, had good eyesight

IV 68 F B M, aged 35, had cataracts The cataracts had been operated on She did office work

IV 70 M B T, aged 40, had good vision

IV 71 W B, aged 30, did not wear glasses and was believed to have good eyesight

IV 72 This person, aged 28, had no trouble with the eyes

IV 73 This person, aged 40, was believed to have good vision

V 1 (fig 12) E H, Jr, aged 12, had cataracts Vision in the right eye equaled 6/20 + 1, in the left eye 6/20 The smallest print he could read was Jaeger's test type 6 at 21 cm with the right eye and Jaeger's test type 5 at 15 cm with the left eye The pupils dilated to 7 mm There was a spherical opacity in the central half of the lens By slit lamp the fetal nucleus was sharply limited and contained large, semitransparent, circular and oval flakes, each flake centered by a dense white opacity These were dispersed in greater numbers toward the periphery of the fetal nucleus In a narrow zone surrounding the nucleus were many minute flakes Peripheral to this was another zone in which were several groups of posterior opaque fibers The corresponding anterior fibers were clear Y sutures were not visible In the adult nucleus and cortex which ophthalmoscopically appeared clear were visible peripherally very fine, radial, linear opacities, forming riders The posterior region of the fetal nucleus was readily visible, containing fewer of the large opacities than anteriorly There was no greater opacity in the center of the fetal nucleus, i e, the embryonic nucleus

V 2 L J, aged 22, in the army, and V 3, D J, aged 14, both had good eyesight

V 4 R F, aged 15, had no visual difficulty

V 5 R R, aged 12, had cataracts Both eyes had been needled before our examination, the right eye unsuccessfully Evidently the operation on the right eye was followed by uveitis and glaucoma The left eye had good vision with a cataract lens

V 6 S R, aged 11, had refraction performed, with paredrine hydrobromide-homatropine hydrobromide used as a cycloplegic Vision in the right eye with a + 1.00 D sph \odot + 1.25 D cyl, ax 90 was 6/12, in the left eye with a + 1.50 D sph \odot + 1.00 D cyl, ax 90, 6/7.5 - 2 There was no phoria The fundi were normal Slit lamp examination of the lenses revealed them to be of average clearness for her age, except in the upper nasal periphery in the right lens, where there was a small opaque flake limited to a definite zone

V 7 In M D, aged 6, and V 8, aged 3, the condition of the eyes was unknown to family

V 9 In J D, aged 12, slit lamp examination through dilated pupils showed clear lenses

V 10 C D, aged 10, had cataracts Vision in each eye was 14/200 With pupils dilated to 7 mm the central half of the lens was a sharply outlined spherical opacity, with a surrounding narrow zone of very fine, powdery spots Farther out in the lens extending to the periphery were fine riders In the nuclear opacity, pearl-like spheroids were scattered irregularly in almost the entire outer third Only occasional spheroids were seen in the deeper zones

V 11 J D, aged 5, and V 12, W D, aged 3, had clear lenses when examined through dilated pupils with slit lamp

V 13 (fig 13) B H, aged 7, had cataracts She had had difficulty seeing her school work Vision in the right eye was 18/200, in the left eye 18/200 Retinoscopy with atropine as a cycloplegic was difficult because of the opacity of the lenses, and glasses did not appreciably improve vision Vision in the right eye

with a -100 D sph $\perp -150$ D cyl, ax 180 was 18/200, in the left eye with a -025 D sph \perp and a -050 D cyl, ax 180, 18/200. The central halves of the lenses were partially opaque spheres surrounded by thin zones of fine punctate opacities. In the center of the lens was a large dense granular opacity sur-

V 14 D H, aged 6, had cataracts. Retinoscopy through dilated pupils was not difficult. The central, spherical, fetal nucleus had evenly scattered white opacities with a less densely opaque oval halo around each (same as fig 13 A, of V 13). These were evenly dispersed through the anterior part of the fetal nucleus.

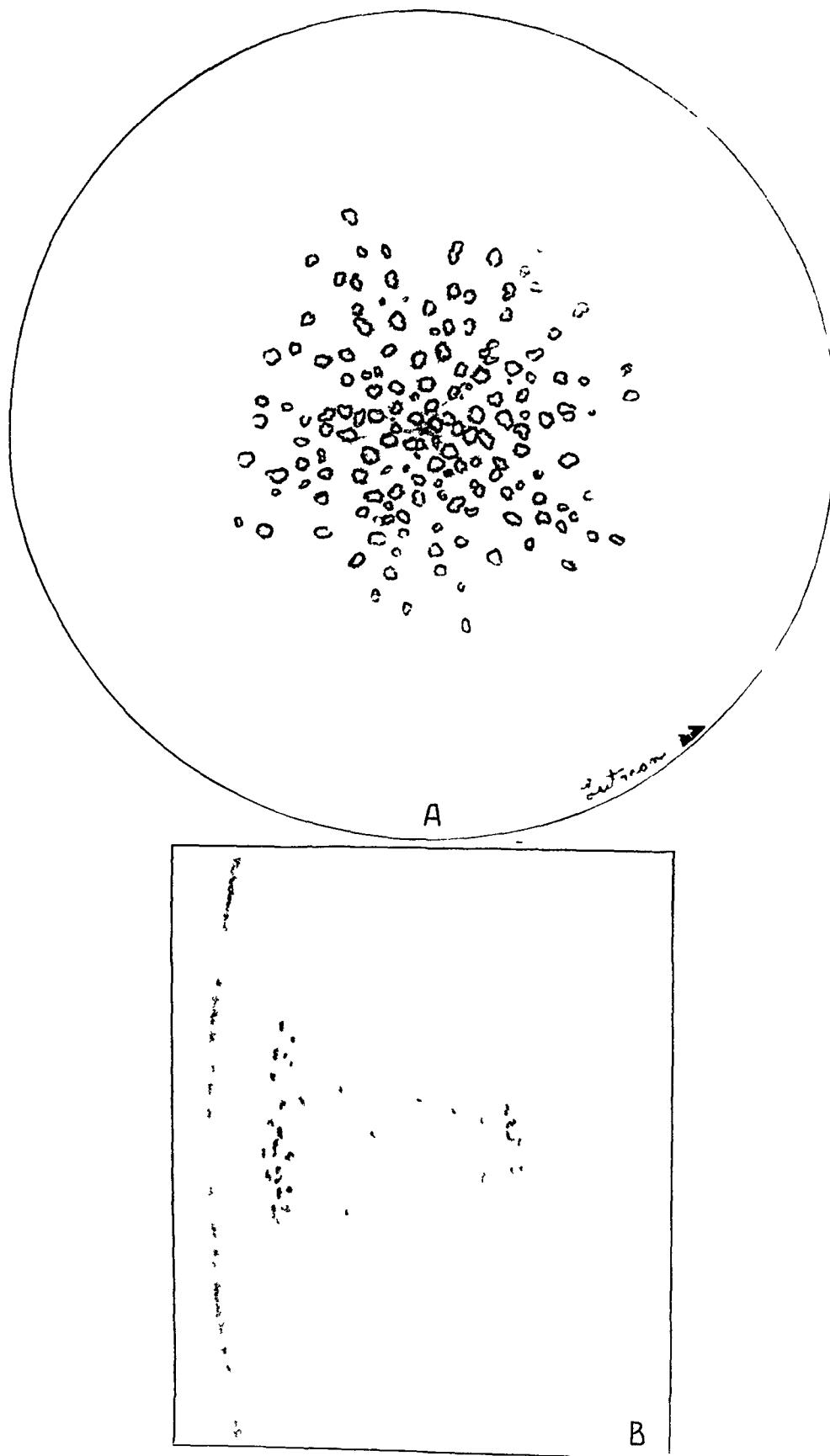


Fig 11.—A, slit lamp view of the cataract in IV 59 (B D, aged 16). B, schematic cross section of the lens in the same person.

rounded by a zone of fine granules and farther out by a dull milky opaque zone. In the anterior layers of the fetal nucleus were large grayish opaque flakes, each with a white center.

The embryonic nucleus was no more opaque than the fetal region. The fetal nucleus was surrounded by a single zone of fine, faint opacities. Vision in the right eye with a -050 D sph $\perp + 375$ D cyl, ax 90

was 6/20—1 in the left eye with a +250 D cyl, ax 90 6/15—1. The fundi were normal.

V 15 In G H, aged 2, slit lamp examination through dilated pupils showed clear lenses. The fundi were normal. Retinoscopic examination gave the following results right eye, +150 D sph \supset +250 D cyl, ax 90, left eye, +150 D sph \supset +125 D cyl, ax 90.

V 16 W C, aged 7, had been examined by an ophthalmologist who did not find cataracts or need of glasses.

V 17 In N C, aged 5, the lenses examined ophthalmoscopically through dilated pupils were found clear. Slit lamp examination showed three minute white flakes in the right eye just in front of the anterior Y suture, and in the left eye two similar flakes.

and change with age. These three types of cataract are:

(1) Fenestrated, flakelike, iridescent opacities and vacuoles located in the axial portion of the anterior adult nuclear zone, with small shining crystals in the deeper zones. With age, vacuoles and clefts developed in the peripheral cortex and adult nucleus. We saw only 4 members of the pedigree who were afflicted with this type of cataract, II 10 (fig 3), in whom the fetal nucleus was outlined, and 3 of her descendants—III 30 (fig 5), III 34 (fig 6) and IV 59 (fig 11).

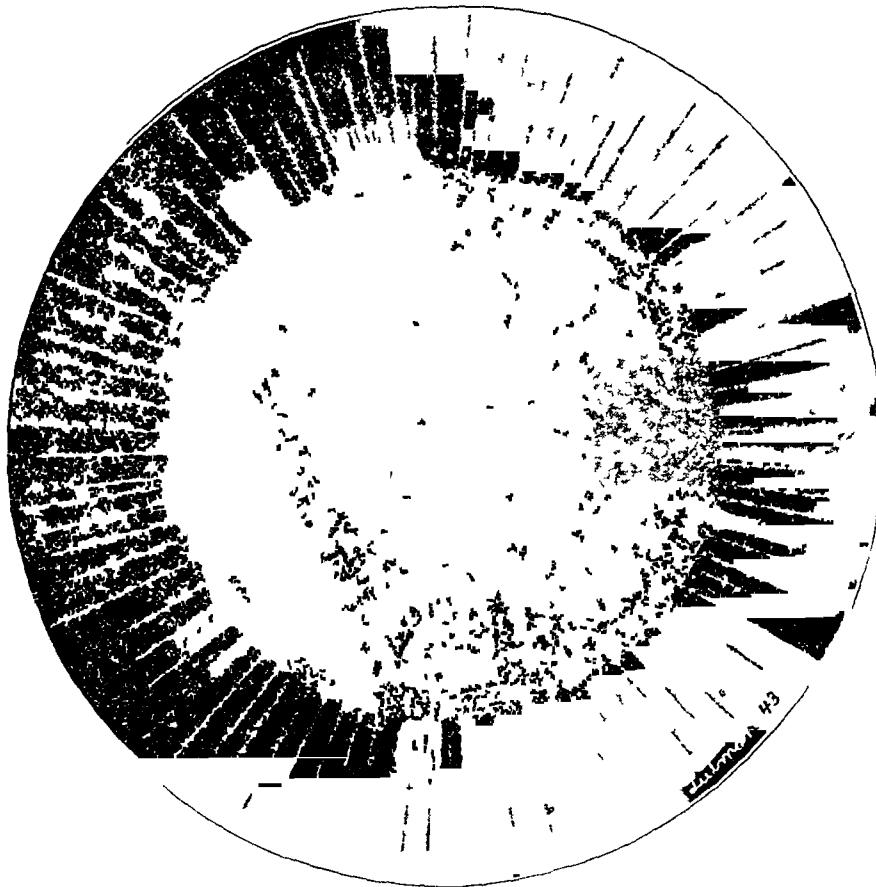


Fig 12.—Slit lamp view of the cataract in V 1 (E H, aged 12)

V 18 In T C, aged 3, the lenses were clear when ophthalmoscopically examined. Slit lamp examination through dilated pupils showed two punctate flakes visible in each eye just before the anterior Y suture.

V 19 M B, aged 8, had good vision.

V 20 In A deB, aged 7, the lenses, examined with slit lamp through dilated pupils, showed an occasional minute opacity, but no more than average.

V 21 E M, aged 13, had good vision.

V 22 and V 23 had no trouble with their eyes.

V 24 and V 25 had no trouble with their eyes.

V 26 B U, aged 18, had cataracts. Both lenses had been needled.

V 27 G M, aged 19, had no visual trouble.

V 28 J M, aged 11, had cataracts. These are believed to have been needled.

V 29 This child, aged 3, is believed to have good eyes.

THE CATARACT

In this genealogy the cataracts fall into three general categories, which are subject to variation

In this line of the family no other type of cataract was present.

(2) An opacity of the fetal nucleus. Such cataract occurred in III 18 (fig 4), with wide variations present in her descendants. In some instances semiopaque flakes were found in the fetal nucleus, each centered by a dense, white spot, as in V 1 (fig 12) and V 13 (fig 13). In other instances (IV 10 and IV 24 [fig 8, B]), distinctly different semitranslucent ovoid opacities were found instead of the flakes. In IV 47 (fig 10), the spheroid opacities of this last type remained unabsorbed on the iris long after the cataract had been needled. The larger flakes and spheres of the fetal nucleus were more numerous in the anterior and peripheral portions. The

flake opacities became more dense with age. Neither type changed into the other with age, and both were found in young persons. The embryonic nucleus contained more dense opacities in some instances (V 13 [fig. 13])

Only once, in IV 24 (fig. 8B), was the anterior Y suture of the fetal nucleus visible.¹² Here it was accentuated as an opaque Y. The sutures of the embryonic nucleus were not visible in any of the cataracts.

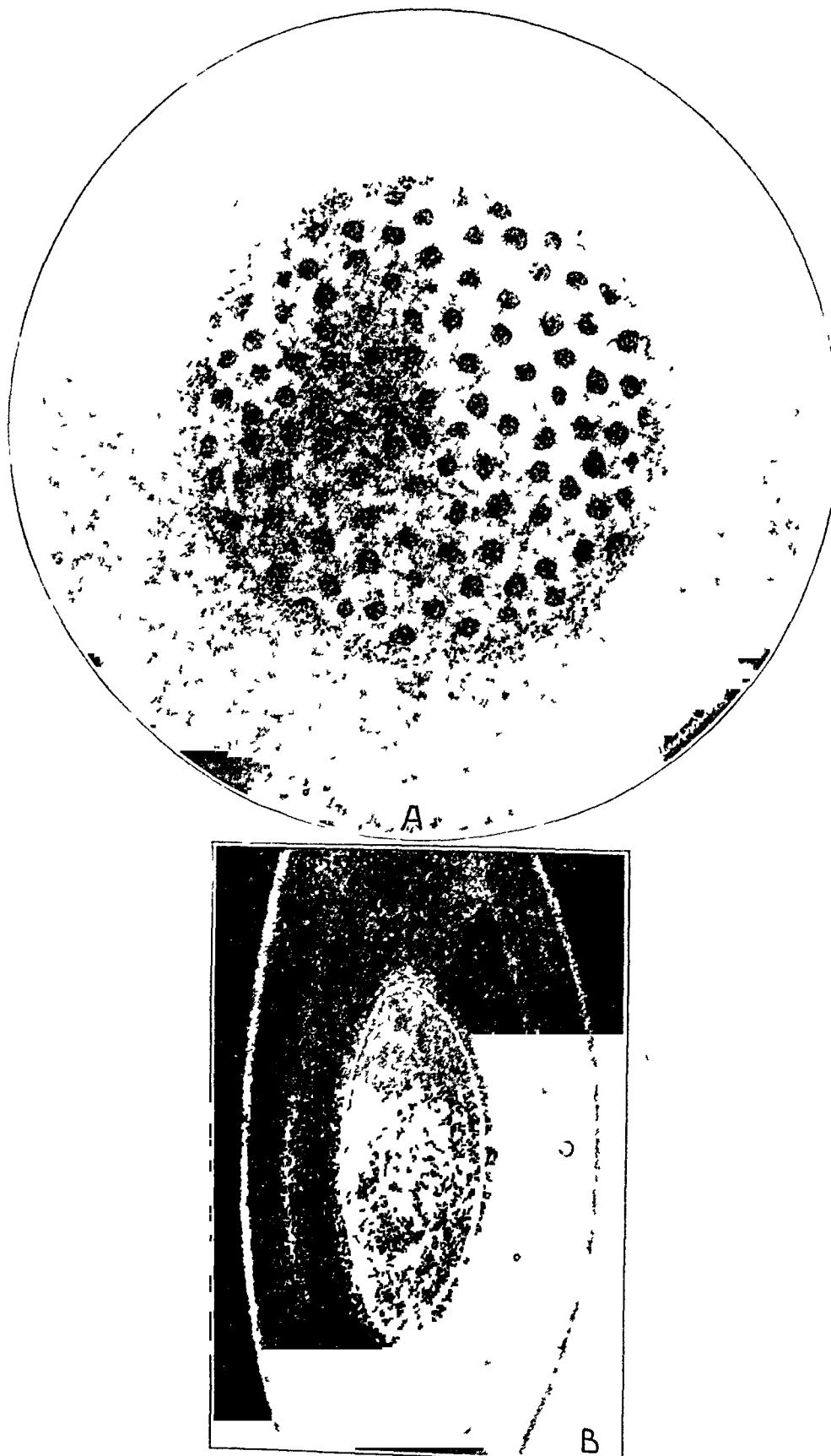


Fig. 13.—A, slit lamp view of the cataract in V 13 (B H, aged 7), B, schematic cross section of the lens in the same person

¹² The Y sutures are located on the central embryonic nuclear surface which is surrounded by the peripheral embryonic nucleus (in this paper referred to as the fetal nucleus). The latter nucleus, corresponding to the time

just before birth and at birth, also shows a simple suture surface (Vogt, A. Atlas of the Slit-Lamp Microscopy of the Living Eye, translated by R. von der Heydt, Berlin, Julius Springer, 1921, p. 58)

In several of the adults (IV 18 [fig 7] and IV 23 [fig 8A]), an anterior polar opacity was present, and continued backward as a fusiform axial opacity to the fetal nucleus. The anterior capsules were normal in all of the cataracts.

Additional zonular opacities occurred in IV 23 (fig 8A) and V 1 (fig 12), and narrow ridges were found in IV 18 (fig 7), IV 24 (fig 8B), V 1 (fig 12) and others.

(3) A feather-like cataract formed by opacification of the lens fibers along the anterior and posterior sutures of the adult nucleus. IV 26 (fig 9) presented such a picture. Except for granular opacities in the embryonic nucleus, no flake opacities were seen in this cataract, which was composed entirely of opaque lens fibers. The children of IV 26 reverted to the fetal nuclear type of cataract (V 13 [fig 13]).

The fetal nuclear opacity (type 2) caused more visual interference, and more rapid opacification took place, than occurred with the fenestrated flake opacity of the adult nucleus (type 1). Thus II 10 retained useful vision longer than the other members of her generation, her son, III 34, at the age of 36 had better vision than most of the children with a nuclear cataract.

The cataracts in all cases examined which had not been subjected to operative treatment were the same in the two eyes. Anatomically every zone and surface of the lens is affected by some form of opacification in one or more persons. The most dense opacities tended to form along the lens axis. In 1 instance (II 6) the lens was found to be a complete opacification.

It is significant that these three types of cataract do not appear to be distributed at random throughout the pedigree. For example, type 1 is present in II 10 and all her cataractous descendants whom we examined, III 18 and most of her cataractous descendants, on the other hand, had a type 2 cataract. However the only person with a type 3 cataract was also a descendant of III 18.

MODE OF INHERITANCE OF THE CATARACT

In any consideration of the inheritance of cataract in this pedigree, the following hypotheses at once arise. 1. All the cataractous persons in this pedigree may have inherited a certain factor which results in the appearance of a developmental cataract, but one or more genetic and possibly environmental modifiers determine to a large extent exactly what type of cataract forms. According to this hypothesis II 6 and her descendants have inherited, for the most part a different set of modifiers than e.g. II 10 and her children although the 'main' fac-

tor for cataract is the same in the 2 persons. In other words, the details of the cataract are to a large extent determined by the genetic milieu in which the factor postulated to be responsible for the appearance of a cataract is deposited. 2. A second possibility is that I 1 had two different genetic factors making for cataract, and that some of his children inherited one factor and other children the second factor. 3. Finally, there is the possibility that the gene for cataract present in I 1 mutated to a new allele, and that some affected children received the new allele, the others, the original factor.

A final decision between these possibilities is not feasible at present. However, in view of the rarity of inherited, developmental cataract, it is improbable that I 1 carried two different genes making for this condition. Moreover, mutation to a new allele, although possible, is likewise rare. The first hypothesis therefore emerges as the most probable—if one grants the existence of genetic and possibly unlocalized environmental factors with effects of the magnitudes observed.

In this connection it is of interest to review briefly some of the other pedigrees in which significant variability in the type of cataract has been observed. In the following review we shall quote the authors concerned wherever possible, since, as will be evident, it is not always clear from the terminology exactly what type of cataract is involved.

Knies⁶ described a pedigree in which the maternal grandfather, mother and 4 of 6 children had cataract. The cataract of the grandfather is described only as cataracta tremulans and accieta. Concerning the mother he writes that “

besonders in der Zone zwischen Kern und hinterer Cortex, aber auch weniger zahlreich zwischen Kern und vorderer Cortex eine Masse lichtgrauer Punkte vorhanden waren” (page 216) (especially in the zone between the nucleus and the posterior cortex was a mass of light gray specks, but they occurred also although less numerous between the nucleus and the anterior cortex). The cataracts of the 4 children do not fit into any simple classification. Those of the first child were mainly a combination of nuclear and anterior and posterior polar cataracts (axial), those of the second, nuclear, and those of the third, a combination of nuclear and posterior discoidal. In the fourth child there were significant differences between the two eyes, the right showing a lamellar type and the left an axial cataract.

Gjersing (1878, quoted from Harman²) studied a cataractous family in which both nuclear and lamellar cataracts were present, with considerable variation in the exact type of each

One 4 year old child is reported to have had a "central lenticular cataract in one eye, and diffuse capsular cataract in the other eye" (Harman,² p 164)

Nettleship,¹ in 1906, reviewed the literature on inherited cataract and presented many new pedigrees. The most interesting case in relation to the present considerations is the Betts genealogy (case 58), involving more than 90 persons, 30 of whom were known to be cataractous. This is predominantly a pedigree of coralliform cataract, but in two different instances a child of a father with coralliform cataract had lamellar cataract. In 1 person, son of a cataractous father whose type is not described, the lens showed "opaque pearl-like bodies" toward the center, the periphery was clear. Concerning the possible relationship between coralliform and lamellar cataract, Nettleship writes "Although it is necessary for descriptive purposes to keep the axial or coralliform apart from the lamellar cataract, it may, perhaps, be found eventually that both arise from the same, or similar, causes operating at different stages, or over longer and shorter periods of foetal life" (p 217). In addition to this one extensive pedigree, he describes the following shorter family histories, all but one previously unrecorded, in which significant differences were noted in the type of cataract present in parent and in child: (1) Hirschberg's case (1876) of a mother with "complete uncomplicated cataract in one eye, and congenital striopunctate cataract in the other" and her daughter with a double-layered lamellar cataract of both eyes (case 63, page 227); (2) a mother with "small stationary lamellar cataracts" and her son with an "irregular axial opacity from center of lens to posterior pole" (case 74, page 231); (3) a mother with "sharply defined anterior and posterior cortical spokes" and her daughter with "small lamellar cataracts just filling moderately small pupils" (case 76, page 232); and (4) a mother with "cortical cataracts, close beneath anterior capsule, in form of fine dots, and large and small spokes, all parts of surface of cortex affected, except anterior pole, which is quite free" and her son "under care for lamellar cataracts" (case 79, p 233).

Two years later, Nettleship^{7b} described the extensive Coppock pedigree. Of 32 cases of developmental cataract in this group, 24 were of the lamellar type and 8 of the discoid variety, the latter characteristically consisting of a small postnuclear opacity of finely granular appearance. In 2 instances 1 member of a pair of siblings had a lamellar and the other a discoid cataract. Nettleship wrote "The conclusion

seems to be that we have more to learn about the relationship between these two forms of cataract, and that a graduated series will probably be found passing from the smallest and faintest disc of intransparency between anterior and posterior pole, to the common lamellar cataract with its well developed anterior and posterior layers and ridges and having a diameter considerably larger than the natural pupil" (p 231).

Harman¹³ has described a family in which "the opacities observed in the lenses were of small size, and vary from complete spherical lamellar opacities of sharply defined contour, to small dense white opacities situated immediately anterior to the lens nucleus, and taking the shape of Y, X or *". The position and general contour of the latter markings suggest the possibility of their being allied to the small forms of the coralliform cataract".¹⁴

Gioenouw,³ in his treatise on disease of the eye as related to disease elsewhere in the body, was apparently the first to suggest clearly that usually one inherits a tendency to cataract rather than a particular type of opacity. "In der Regel vererbt sich nur die Linsentrubung im allgemeinen, nicht eine besondere Form der Katarakt" (p 701) (As a rule only the opacity of the lens in general is inherited, not any special type of cataract). In support of this hypothesis he quoted Hirschberg (1876), Knies (1877), Becker (1883), Kunn (1889), Nolte (1896) and Hosch (1897), but gave no particulars concerning the work of these men. The papers by Hirschberg (1876, quoted from Nettleship¹) and Knies⁶ have already been described. That by Kunn¹⁵ does not contain sufficient data to offer significant support for the hypothesis. We have been unable to verify the other references. Gioenouw himself found among the seven children of a father operated on for lamellar cataract two "welche angeborene Trübungen in den vorderen und hinteren Rindschichten der Linse, allerdings nicht von der Form eines typischen Schichtstaates zeitgen" (p 702) (who showed congenital opacities in the anterior and posterior layers of the lens, but they were not in form of typical lamellar cataract).

Halbertsma⁹ briefly described a pedigree of 95 persons, 92 of whom he examined and 49 of whom had cataract. The defect occurred in two principal forms "(a) Cataracta coerulea punctata ant et post, (b) perinukleare Cataracta

¹³ Harman (footnotes 2 and 8, fig 307)

¹⁴ Harman,² p 142

¹⁵ Kunn, C G Vererbung des Schichtstaates in einer Familie, Wien klin Wehnschr 2 49, 1889

zonularis" (p 108) No further descriptions of the cataracts are given, nor is a detailed pedigree presented.

The pedigree of Welsh and Wegman¹⁰ is comparable to that of Knies⁶ in the variety of forms which the cataract may assume. The pertinent observations cover four generations and include 20 persons. The 6 affected males showed an irregular, lamellar type of cataract associated with tiny white dots in the cortex. In the 6 affected females opacities tended to develop along the posterior embryonic suture and in the posterior Y suture. In some females other defects of the lens coexisted with these opacities. Thus, in 2 persons there were faint central opacities in one lens, while in a third many punctate opacities were scattered throughout the central portion of the lens. The family represented an intermixture of white persons, Negroes and Indians.

In none of these studies can we be certain as to which of the three hypotheses outlined in connection with the present pedigree is correct. However, in view of the rarity of inherited cataract and the infrequency of mutation, it is improbable that any large proportion of these pedigrees represent either mutation or the chance association of two different factors each resulting in cataract. We are therefore led to seek the explanation in the occurrence of genetic or environmental modifiers.

The finding of significantly different types of cataract in the two eyes of one person (Knies⁶; Gjersing, 1878, quoted from Hartman²) suggests that chance or asymmetrically distributed developmental factors may be important, barring, of course, somatic mutation, which is rare. That genetic modifiers can also create differences of the magnitude observed here is well known from experiments with laboratory animals such as *Drosophila*, the mouse and the guinea pig. The actual demonstration of the action of genetic modifiers in the human species is difficult because of the impossibility of making the requisite crosses. However, a case in point has been described by Mohr and Wriedt¹⁶. They studied the inheritance of a type of brachyphalangy in a large family group, finding that the characteristic was inherited as if due to a dominant factor. The malformation occurred in two fairly distinct forms, one more extreme than the other, one form prevailing with few exceptions in one line of the family, and the other form prevailing in another line. They suggest that the difference between the two forms may be due to a dominant

modifying factor. The similarity of this case to that described here is striking. Recently Stiles and Pickard¹⁷ briefly described a pedigree of variable malformations of the hands and feet which is perhaps comparable to the one presented here. In none of these examples can we adequately separate the role of genetic and environmental modifiers but if the latter play an important part they probably exert most of this effect early in the development, i.e., prenatally. As yet little is known concerning the importance to morphogenesis of variations in the intrauterine environment. In the formation of developmental cataract, one must assume that the genetic and environmental modifiers exert their influence to a variable degree throughout the life of the individual, on the developing as well as on the formed portion of the lens.

Assuming then, that in the present pedigree the occurrence of cataract has the same genetic basis in all affected persons, the question arises as to the type of inheritance involved. It is obvious that here, as in most pedigrees of inherited cataract a dominant factor is at work. Transmission is direct, from affected to affected. In the entire pedigree there are twenty-four marriages between a normal and a cataractous person, resulting in 79 children: 34 normal, 43 cataractous and 2 of unknown type. This is in agreement with the 1:1 ratio expected from a dominant factor. There are 23 affected males and 20 affected females. Little can be said at present about the nature of the modifying factors which are responsible for the differences between the various types. It is worth pointing out, however, that if the differences between the cataracts of II 6 and II 10 were due to the action of a single, nonlinked autosomal dominant modifier present in II 10 (the simplest genetic hypothesis possible), the chance that her 3 cataractous offspring would inherit this modifier is 1 in 8—a figure well within the bounds of probability. If the differences were due to a sex-linked dominant modifier, then the chance that both the sons of II 10 would receive this factor is 1 in 4, and since any male with such a factor automatically transmits it to his female offspring, IV 59 would of necessity receive the modifier from her father.

COMMENT

In the past it seems to have been for the most part more or less tacitly assumed that a different genetic factor was responsible for each of the almost multitudinous types of developmental

¹⁶ Mohr, O. L., and Wriedt, C. A New Type of Hereditary Brachyphalangy in Man, Publication 295, Carnegie Institution of Washington, 1919.

¹⁷ Stiles, K. A., and Pickard, I. S. Hereditary Malformations of the Hands and Feet, Rec Genet Soc America **12** 55, 1944.

cataract that have been described. It is probable that many different genes do affect the structure of the lens. However, from the foregoing considerations the strong possibility emerges that in at least some of these various pedigrees the "main" genetic factors involved may be the same, with the differences due to the action of modifying genetic and environmental factors. In other words, we are led to a genetic concept of inherited cataract which postulates the existence of a number of different factors whose exact expression is subject to the action of modifying genes, and possibly environmental determinants rather than to the concept of numerous specific genes each determining a fixed type of cataract. In ethnologically diverse groups the same factor may be expressed differently. If important modifying factors happen to be segregating within a given family, significantly different types of cataract may occur in the members of this family. If no such segregation is occurring, uniformity of type exists—and this happens to be the situation in the majority of pedigrees. In a sense this viewpoint may be regarded as an amplification of the hypothesis advanced by Grootenhuis in 1920 and quoted by us. It is possible that Duke-Elder¹⁸ had essentially the same thing in mind when he wrote:

When the intricacy of the architecture of the lens is remembered with its complex lamellar and sutural arrangements, it will be realized that a whole host of morphological types of developmental cataracts with little fundamental distinction are potentially possible. Their essential similarity is emphasized by the fact that in their hereditary transmission one type may replace another in the pedigree (p. 1365).

Considerable has been written, especially by the German authors, concerning the eugenic aspects of inherited cataract, and the possible desirability of sterilizing persons so afflicted. The steady improvement in surgical technics for dealing with this condition makes the considerations of twenty to thirty years ago outmoded. After operation these patients can successfully engage in all but the visually most demanding types of work. As was pointed out in the description of the family, the cataractous members comprising the present pedigree have in no

sense been a drag on their community. The society which denies such people as these the right to propagate takes advantage of the presence of a readily recognized and simply inherited characteristic, while ignoring the presence of numerous other equally or more undesirable but less obviously inherited traits whose genetic bases have not yet been worked out. However, it is recognized that the cataractous members of this group may not be typical of persons found in the majority of families with developmental cataract.

SUMMARY

In a genealogy extending over 5 generations and comprised of 123 people 44 had cataracts from childhood onward. Thirty-four of these 123 persons were examined by the authors. 21 of those examined had cataract.

Three distinct types of cataract can be recognized among the affected persons as follows: (a) fenestrated opaque flakes predominantly in the axial region of the anterior adult nucleus, (b) a fetal nuclear opacity containing either flakes or spherical bodies with numerous variations in the lens opacities accompanying this, and (c) opaque lens fibers, most prominent adjacent to the adult lens sutures. The third type was seen in only a single person.

Type (a) was found to the exclusion of other types in one line of the family, while type (b) greatly predominated in another branch.

Three hypotheses for the occurrence of distinct types of cataract within a single pedigree are advanced, namely: (a) the existence of genetic and environmental modifiers which bring about variations in the expression of a "main" factor, (b) the simultaneous presence in the founder of the line of two different, independently inherited factors responsible for cataract and (c) the occurrence of mutation.

It is concluded that the bulk of the data, both our own and that in the literature, is best explained by the first hypothesis.

Mrs James Neel drew the pedigree, and Mr N C Jacobs, medical illustrator, and Mr M C Orser, medical photographer, gave valuable advice in helping us to prepare the figures.

¹⁸ Duke-Elder, W. S. *Text-Book of Ophthalmology*, St Louis, C V Mosby Company, 1938, vol 2

SURGICAL MANAGEMENT OF GLAUCOMA IN CORRELATION WITH GONIOSCOPY AND BIOMICROSCOPY

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The correct surgical management of glaucoma is still an unsettled problem. This paper deals with the limited aid which gonioscopy and biomicroscopy can offer the clinical ophthalmologist in a rational approach to the surgical treatment of glaucoma. It is a summary of our experience with patients of the Meyer Service who have been followed in the glaucoma clinic of the Illinois Eye and Ear Infirmary.

SO-CALLED PRIMARY GLAUCOMA

Acute Glaucoma, Chronic Congestive Glaucoma, Narrow Angle Glaucoma—The onset of acute glaucoma is manifested by severe pain, with pronounced congestion of the eye and occasional chemosis. Occasionally there may be various degrees of congestion in chronic congestive glaucoma.

Acute primary glaucoma presents a grave ophthalmologic emergency, owing to its fulminating character. Its most important characteristic is the presence of a shallow anterior chamber or a narrow angle. If the chamber is normal or deep, the condition is probably not acute primary glaucoma. Hemorrhagic glaucoma and glaucoma rubrum may first become manifest as an acute attack. However, with these types of glaucoma the anterior chamber is usually deep or normal and the iris is congested. There is also commonly a history of previous decrease in vision. Iritis or uveitis may produce an acute attack, but secondary acute glaucoma must be differentiated from primary glaucoma. In this differentiation gonioscopy and biomicroscopy play an important role. If corneal edema is present and examination of the anterior chamber is difficult the cornea may be cleared sufficiently for observation by instilling 1 drop of ordinary glycerin, as advocated by Cogan.¹

The duration of the attack, the visual acuity and the immediate response to intensive therapy with miotics will determine whether one should

or should not operate. The choice of a proper type of operation to control the tension within normal limits is important. An attempt should always be made to lower the tension with a miotic before any type of operation is tried, as extremely hard eyes do not respond well to surgical intervention. If there is no response to intensive instillation of a miotic in a few hours and if this absence of response is accompanied with a considerable decrease in visual acuity, operation must be performed immediately.

The biomicroscopic findings are as follows: corneal edema (although this may be absent), a shallow anterior chamber, congestion of the iris, liberation of iris pigment, which may be scattered over the surface of the iris and sometimes over the capsule of the lens, and powdering of the corneal endothelium. Ordinarily the acuity of the angle may be determined with the biomicroscope by placing the slit lamp beam perpendicular to the cornea at the site of the angle of the anterior chamber and the corneal microscope at the angle of specular reflection and focusing it first on the posterior surface of the cornea and then on the anterior surface of the iris.²

The gonioscopic findings suggest the term narrow angle glaucoma. Sugar³ observed that the angle is open, although narrow, at the beginning of the first attack but is closed during the attack and that the extent and firmness of the peripheral anterior synechias vary directly with the duration of the attack.

Surgical Management The essential evidence obtained with the biomicroscope and the gonioscope is that the angle of the anterior chamber is narrow, and the acuity of the angle depends largely on the extent of the peripheral synechias anteriorly. The surgical problem is, therefore, to enter the anterior chamber with minimum danger to the iris and the capsule of the lens and to avoid sudden decompression of an eyeball with a high intraocular pressure.

This can be accomplished by making a scratch incision or an incision from the outside after a conjunctival flap has been dissected to the limbus.

² Sternberg, P To be published

³ Sugar, H S Concerning the Chamber Angle
I Gonioscopy, Am J Ophth 23:853, 1940

From the Illinois Eye and Ear Infirmary

Read at the Forty-Ninth Annual Meeting of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct 11, 1944

¹ Cogan, D C Clearing of Edematous Corneas by Glycerin, Am J Ophth 26:551, 1943

The scratch incision, made with either a Lundsgaard knife or a keratome, can be beveled to any degree in order to enter an anterior chamber with an extremely narrow angle. The incision may be enlarged with corneal scissors. This type of incision provides for slow decompression, and ordinarily prolapse of iris tissue occurs, also, with this type of incision one avoids entering the chamber with sharp instruments. An incision may be made with a small keratome or a Graefe knife if preferred, provided the anterior chamber is not extremely shallow. Retrolbulbar injection of 1 cc. of 2 per cent solution of procaine hydrochloride with a few minims of a solution of epinephrine hydrochloride (1:1000) is always given just prior to all surgical operations for glaucoma, but this dose is not always adequate for sufficient lowering of the tension. One should always wait five to ten minutes for adequate anesthesia and a possible decrease in tension.

Iridencleisis is to be preferred to the classic basal iridectomy of von Graefe¹ as the treatment for narrow angle glaucoma. The rationale of iridectomy is still a matter of much controversy. It is generally held, as originally suggested by Weber,⁵ that the main effect is the mechanical opening of a closed angle and that the operation is successful only in so far as it accomplishes this and if the iris is removed so completely that blocking of the angle cannot recur. However, the inflammatory reaction, together with contact of the iris tissue with the walls of the angle during the immediate postoperative period before the shallow anterior chamber has reformed, may contribute to additional peripheral anterior synechias. Kronfeld⁶ stated that the smallest sector of open angle compatible with normal intraocular pressure is 70 to 90 degrees of arc.

The mechanical concept does not furnish the complete explanation, for gonioscopic examination has shown that the results are successful in many cases if the base of the iris is left and is poor if the base is totally removed (Uribe Troncoso⁷, Werner⁸). Among many other explanations, these suggestions have been made. The vasomotor reflexes are abolished (Abadie⁹),

a filtering scar is formed accidentally, with or without the incorporation of uveal tissue (de Wecker¹⁰), since a wound in the iris does not cicatrize (Fuchs¹¹), a permanent flesh absorbing surface is exposed to the aqueous.

Since the rationale of iridectomy is controversial and since it has been shown by Uribe Troncoso,⁷ Thorburn,¹² Werner,¹³ Barkan¹⁴ and McLean¹⁵ that the peripheral anterior synechias are a result, and not the cause, of glaucoma and that, therefore, the cause of narrow angle, or acute congestive, glaucoma is not entirely "mechanical," the factors involved in the other types of primary glaucoma may be prevalent here as well. It seems ill advised, therefore, to depend on the mechanical concept of making the normal drainage channels available through iridectomy. True, iridectomy is frequently successful, but we believe iridencleisis is the more logical procedure. Basal iridectomy, if preferred, should be done during the first attack of acute glaucoma and if the attack is of less than twenty-four hours' duration.

The narrow angle and the effects of the narrow angle offer a sufficient mechanical hazard during operation and afterward to make trephination a poor choice. It is necessary that the trephine opening be placed sufficiently anteriorly in the cornea to avoid the formed peripheral anterior synechias and ciliary incarceration, and this in itself is difficult. In attempts to do this, a flap consisting not only of the corneal epithelium but of the epithelium and the corneal stroma is dissected, when the flap is replaced after the trephination, corneal stroma becomes firmly anchored to corneal stroma, with prompt closure of the trephine opening. The technical difficulties and the accidental injuries which can occur with the trephination need no mention.

Chronic Simple Glaucoma, Glaucoma Simplex, Wide Angle Glaucoma—Glaucoma simplex is characterized by certain changes in the visual fields, increased intraocular tension, especially

10 de Wecker, L. *Traité théorique et pratique des maladies des yeux*, Paris, A Delahaye, 1867, vol 2, p 571.

11 Fuchs, E. *Ber u d Versamml d ophth Ge-sellsch* 25:179, 1896, cited by Duke-Elder, W S *Text-Book of Ophthalmology*, St Louis, C V Mosby Company, 1941, vol 3, p 3401.

12 Thorburn, A. *A Gonioscopic Study of Anterior Peripheral Synechiae in Primary Glaucoma*, Thesis, Stockholm, 1927.

13 Werner, S. *Gonioscopical Studies of Operated Cases of Glaucoma*, *Acta ophth* 10:112, 1932.

14 Barkan, O. *New Operation for Chronic Glaucoma Restoration of Physiological Function by Opening Schlemm's Canal Under Direct Magnified Vision*, *Am J Ophth* 19:951, 1936.

15 McLean, J. *Gonioscopy in Glaucoma Operations*, *Tr Am Acad Ophth* 45:176, 1941.

4 von Graefe, A. *Ueber die Iridectomie bei Glaucom und über den glaucomatosen Process*, *Arch f Ophth* 3(pt 2) 456, 1857.

5 Weber, A. *Die Ursache des Glaucoms*, *Arch f Ophth* 23(pt 1) 1, 1877.

6 Kronfeld, P C. *In Search of Gonioscopic Correlates of Responsiveness to Miotics*, to be published.

7 Uribe Troncoso, M. *Gonioscopy and Its Clinical Applications*, *Am J Ophth* 8:433, 1925.

8 Werner, S. *Gonioscopic Studies on Glaucomatous Eyes Following Operation*, *Finska laksallsk handl* 73:981, 1931.

9 Abadie, C H. *Section de la zone ciliaire ou cilioretinotomie*, *Arch d'ophth* 30:262, 1910.

during the early morning hours, and various degrees of cupping of the optic disk. If these changes cannot be held in check with the use of mild miotics, surgical treatment is indicated.

The biomicroscopic findings ordinarily do not differ from the normal unless vascular compensation occurs. Varying degrees of atrophy (of the iris), however, may be present.

The gonioscope reveals exclusion of the narrow angle mechanism hence the term wide angle glaucoma. Other gonioscopic findings are deposits, of varying amounts of pigment, within the corneoscleral trabecula, decreased translucency of the trabecula or trabecular sclerosis, and peripheral anterior synechias in late stages. Kronfeld, McGarry and Smith¹⁶ observed an abnormal filling phenomenon of Schlemm's canal after paracentesis of the anterior chamber or massage of the eyeball.

Surgical Management The successful surgical management of wide angle glaucoma depends on the functional efficacy of new outflow channels. The presence of peripheral anterior synechias before or after operation does apparently alter the efficacy of these new outflow channels to some extent.¹⁵

Iridencleisis is preferred except when atrophy of the iris is present. This is a much less difficult procedure technically and can be done with less chance of accidental damage to important structures. It is, therefore more applicable to use by the average as well as by the expert operator.

However, trephination may be done if it is preferred, since with wide angle glaucoma there is "sufficient room" in the angle for the procedure. It is definitely the operation of choice when atrophy of the iris is noted.

Cyclodialysis will be discussed subsequently.

GLAUCOMA FOLLOWING REMOVAL OR CATARACT

This form of glaucoma was shown by Czermak¹⁷ to result from peripheral anterior synechias due to delayed restoration of the anterior chamber after cataract extraction. This cause was confirmed gonioscopically by Sugar³ and by Kronfeld and Grossman¹⁸. The extent and the firmness of the peripheral anterior synechias vary directly with the duration of the contact of the iris root with the wall of the angle.

¹⁶ Kronfeld, P. C., McGarry, H. I. and Smith, H. E. Gonioscopic Studies on the Canal of Schlemm, Am J Ophth 25:1163, 1942.

¹⁷ Czermak, W. Die augenärzliche Operationen, Vienna, C. Gerold's Sohn, 1898.

¹⁸ Kronfeld, P. C., and Grossman, E. E. The Relation of the Gonioscopic Findings to the Incidence of Secondary Glaucoma in Operative Aphakia Tr Am Acad Ophth (1940) 45:184, 1941.

The gonioscope reveals closure of the angle, with peripheral anterior synechias of varying extent. Kronfeld and Grossman¹⁸ stated the belief that the blue or gray iris forms synechias characterized by fuzzy edges, while the brown iris with the dense anterior border forms synechias with solid line edges, as viewed with the gonioscope.

Surgical Management Although in some cases this form of glaucoma may respond well to a miotic, tolerance to the drug seems to occur within a relatively short time, and surgical treatment will finally be required in many cases.

With regard to cyclodialysis, Barkan¹⁹ and Sugar³ noted an "all or none" relation between the success of the operation and the formation of a communication between the anterior chamber and the supraciliary space, which can be seen as a definite cleft with the gonioscope. McLean²⁰ showed that the success of the cyclodialysis varies directly with the acuity of the angle and the depth of the anterior chamber. Therefore, cyclodialysis is usually not advocated for narrow angle glaucoma and is advised only on occasion for wide angle glaucoma, particularly when associated with low elevated tension, or as a secondary operative procedure for wide angle glaucoma with slightly elevated tension following a previous partially successful filtering operation. Its greatest efficacy for glaucoma is after removal of a cataract. Many well performed cyclodialyses fail because of the organization of a blood clot in the cleft. The avoidance of the horizontal meridian, where the posterior ciliary vessels and nerves are located, and the use of physostigmine after operation will minimize this complication. Observance of Gradle's²⁰ suggestion that the operation be done in one of the upper quadrants and that the patient sit up in bed after operation will tend to keep blood out of the cleft if hemorrhage occurs. The limbs of the coloboma should be avoided to prevent unnecessary trauma and hemorrhage. If cyclodialysis fails, it may be repeated. If it fails again, trephination may be tried.

A means of preventing formation of peripheral anterior synechias with delayed restoration of the anterior chamber after cataract extraction, is the use of an adequate corneoscleral suture at the time of the cataract extraction.¹⁵ Another means is postoperative injection of air into an unrestored chamber, as advocated by McLean,¹⁷ MacMillan²¹ and others.

¹⁹ Barkan, O. Mode of Action of Cyclodialysis, Am J Ophth 19:21, 1936.

²⁰ Gradle, H. S. Personal communication to the author, cited by Sugar³.

GLAUCOMA ASSOCIATED WITH CAPSULAR EXFOLIATION

Glaucoma is not present in all eyes with senile capsular exfoliation, hence, the term glaucoma associated with capsular exfoliation is preferred, rather than glaucoma capsulare.

The biomicroscope reveals white, crustlike flakes as a central disk on the anterior surface of the lens corresponding in extent to a minimum dilatation of the pupil, and as a granular girdle about the periphery, with a clear band between the two areas and deposition of these flakes on the iris and cornea.

The gonioscope shows depositions of these fine flakes throughout the structures of the angle, usually accompanied with heavy pigmentation of the trabecula. The angle is of the wide type, with relative absence of peripheral anterior synechias.

Surgical Management—Successful surgical management depends on producing new channels of outflow. Iridencleisis or trephination may be done, since the angle is usually wide. Iridencleisis is preferred for the same reasons as those obtaining in treatment of wide angle glaucoma.

When the lens is sufficiently opaque to warrant cataract extraction and the glaucoma is not controlled with use of miotics, it is advisable to do the operation for glaucoma first. After the eye has completely recovered the operation for cataract may be performed, with extraction of the lens through an incision placed below, temporally or anteriorly in the cornea, provided the antiglaucoma bleb does not overhang too far anteriorly on the cornea.

HEMORRHAGIC GLAUCOMA

Hemorrhagic Glaucoma Following Occlusion of the Central Retinal Vein—The biomicroscope reveals neovascularization of the iris, in addition to many or all of the features of acute congestive glaucoma.

The gonioscope reveals an open angle at first, with considerable congestion and neovascularization of the root of the iris. Somewhat later the angle becomes completely closed.

The surgical management will be considered along with that of diabetic rubeosis iridis.

Diabetic Rubeosis Iridis—Biomicroscopically and gomoscopically the appearance of rubeosis iridis diabetica is similar to that of glaucoma following obstruction of the central retinal vein.

21 MacMillan, J. A. Air Injection as a Factor in Maintaining Filtration Following Corneo-Scleral Trephining in Glaucoma, *Tr Am Ophth Soc* 37:127, 1939.

The angle is closed and covered with formations of fine new vessels.

Surgical Management—For this type of glaucoma, we prefer cyclodiatery puncture of the ciliary body, as described by Vogt.²² The inferior half of the pars corona of the ciliary body is treated with diathermy. The tension is lowered, although not always to within normal limits, but freedom from pain nearly always occurs within thirty-six hours after the operation. Because of the scleral "shrinkage," with resultant decrease in the total volume capacity of the eyeball, which follows the diathermy, extensive diathermy over the complete circumference of the pars corona may raise the intraocular pressure during the immediate postoperative period above the systolic blood pressure in the central retinal artery, with resulting occlusion of the artery; this occurred in 1 case at the infirmary. No case of sympathetic ophthalmia has occurred as a result of this procedure in well over 100 cases at the infirmary in which cyclodiatery was performed.

Enucleation is, of course, the alternative surgical procedure.

GLAUCOMA ASSOCIATED WITH LENTICULAR INTUMESCENCE

Swelling of the lens produces narrowing and later actual blockage of the angle by the root of the iris.

The biomicroscopic and gomoscopic pictures are the same as those for acute glaucoma except for the lenticular intumescence.

Surgical Management—The surgical management resolves itself into removal of the lens. This is accomplished after the chamber is entered by means either of a scratch incision or of an incision made with a small keratome and enlarged with scissors. In this manner one avoids sudden decompression as well as traumatic injury to the iris or lens.

SUMMARY

Gomoscopy and biomicroscopy can be of limited aid in the surgical management of the various types of glaucoma. These clinical instruments present evidence with which the ophthalmologist may better evaluate the type and site of the glaucoma and determine a rational surgical approach to the glaucoma in the individual case.

58 East Washington Street

22 Vogt, A. Versuche zur intraokularen Druckherabsetzung mittelst Diathermieschädigung des Corpus ciliare (Cyclodiatermiestichung), *Klin Monatsbl f Augenhe* 97:572, 1936.

PATHOLOGIC PHYSIOLOGY OF CONVERGENT STRABISMUS

MOTOR ASPECTS OF THE NONACCOMMODATIONAL TYPE

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I accepted with both reluctance and pleasure the invitation to deliver this the first Gifford Memorial Lecture. You can appreciate how difficult it is to prepare a lecture adequate for this occasion, for Sanford Gifford will always live in our memories through his own contributions to our literature.

He wrote with a profound factual knowledge, with the intuition and acumen of a skilled investigator and with a clinical wisdom which comes only from a rare combination of intelligence and common sense—in short, his writings show all the qualities of genius and will themselves constitute a splendid and an enduring memorial.

None of us, I am sure, could ever feel competent to add luster to his fame by any of our own works, but all of us would be most grateful for an opportunity to add our tribute, however small, to the memory of one for whom we had such great affection and high esteem. It is for this opportunity that I thank you most sincerely.

Convergent strabismus is not a single entity produced by one etiologic factor but is an abnormal position of the visual axes due to a number of different causes. Therefore no single theory of the cause of convergent strabismus satisfactorily explains all of the cases one sees.

Donders' accommodative theory fits the largest number, in some of the cases the squint is undoubtedly of paralytic origin, but many others do not fall into either of these groups. Worth's conception of congenital absence or failure of development of a fusion sense as a fundamental factor in the causation of squint conflicts with the fact, widely recognized today, that many of the patients acquire some degree of fusion, and a few even develop stereopsis, after their eyes have been straightened. In addition to this, his theory still leaves unanswered the important question of what causes the abnormal convergence of the visual axes. It will be remembered that Worth insisted that there were two essential conditions

present in every case of comitant convergent squint (1) "an abnormal convergence of the visual axes, (2) a defect of the fusion faculty."¹

The stress which Chavasse² laid on the development of the normal reflex association of the eyes has focused attention on squint as being a perversion of these reflexes, due to any obstacle which dissociates the eyes, and to this I heartily agree. He enumerated some of the motor and sensory obstacles which might prevent or break up the association of the two eyes in the period in which these reflexes are forming. He stated the belief that in many of these cases the squint is due to paralysis of ocular muscles which have recovered.

TABLE 1—Classification of 232 Cases of Convergent Squint According to Cause

Type of Squint	No of Cases	Percentage
Accommodative		
A Completely	62	27
B Partially	69	29
Paralytic	34	15
Undetermined	67	29
Total	232	100

If one leaves out the cases in which squint is the result of paralysis of ocular muscles, all squints are due fundamentally to an abnormal convergence innervation. The group of accommodative squints is the best example of this. It is not necessary to recite the mechanism by means of which an abnormal amount of hyperopia causes squint during the early formative years, by the excessive convergence impulses.

But in only about a third of the cases one sees is the squint wholly accommodative. In table 1 are classified 232 cases of convergent squint from the records of my private cases according to the causative factor.

In about one third of these cases the squint was of undetermined origin. Cases were put in this group only after it was apparent that they could not fit into one or the other of the groups.

1 Worth, C. Worth's Squint, ed 5, Philadelphia, P Blakiston's Son & Co, 1921.

2 Chavasse, in Worth,¹ ed 7, 1939.

ie there were no signs of past or present paralysis of oculai muscles the angle of squint was the same for distance and for near vision , glasses did not change the angle of squint, and the amount of hyperopia present was normal for the age

In the majority of these cases there was complete disappearance of the squint when the patient was under anesthesia. The operative notes show that in many instances the eyes were divergent under the anesthesia before the operation was commenced. This is also true of the other types of squint, accommodative and, in some instances, paralytic, but this fact does not alter the conclusion which one must draw, i.e., that these squints, like the accommodative type, are due to an abnormal convergence innervation. The only difference between the two forms is that in one the source of the abnormal convergence innervation is known i.e. excessive accommodation, whereas in the other form one is as yet totally ignorant of where the abnormal convergence comes from or what it is due to.

If one inquires into the possible sources of abnormal convergence tone, one finds that knowledge of the mechanisms by means of which the ocular muscles are supplied with normal tonic impulses is very sketchy.

It is the primary purpose of this paper to review the normal physiologic mechanism which coordinates the movements of the eyes, in the hope that it will throw some light on the etiologic factors in this large group of cases. For purposes of description, the voluntary movements will be dealt with separately from the involuntary, or reflex, movements but it should be understood that the two mechanisms operate simultaneously and harmoniously.

VOLUNTARY CONTROL OF OCULAR MOVEMENTS

Voluntary movements of the eyes occur as the result of incoming sensory impressions which give rise to a conscious desire to change the position of the eyes, or as the result of impressions that have been received in the past and stored away in the areas of the cortex having to do with memory. The latter when they reach the level of consciousness, again call for volitional movement. Willed movements are usually purposeful ones and call into play many mechanisms which must be coordinated. Whatever the incentive may be to execute a cooordinated muscular movement, it starts in the motor cortex as an excitation of the large pyramidal cells of the pre-central convolution, the so-called Betz cells.

Cortical Centers for Lateral Gaze—In the case of willed ocular movements the pyramidal cells

of the caudal extremity of the second, and possibly the third, frontal convolutions of each hemisphere initiate the action. According to Penfield and Erickson,³ stimulation of a zone which centers on Vogt's area 8 (alpha, beta, gamma), shown in figures 1 and 2, causes conjugate deviation of the eyes to the opposite side and often upward deviation. These movements result from mild stimulation which does not cause convulsive movements. Movements, and

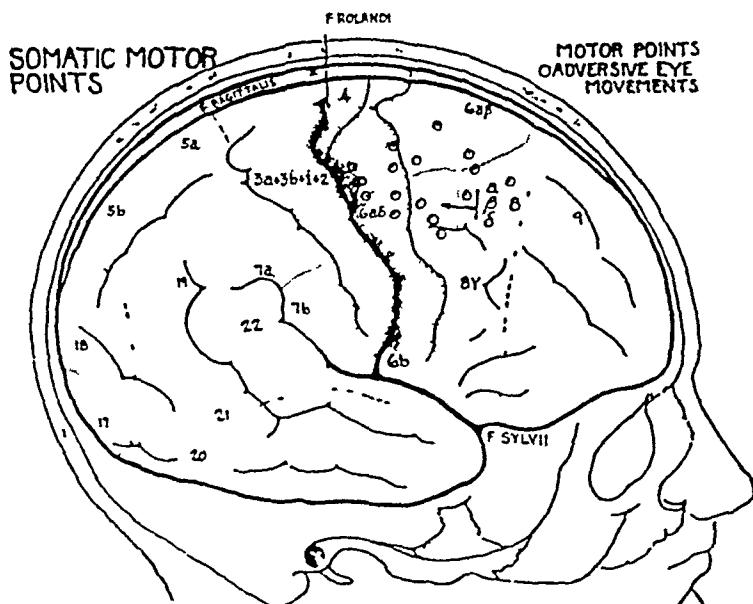


Fig 1.—Surface view of the right motor cortex, showing the areas where stimulation in the conscious subject produced conjugate lateral deviation to the left. Occasionally upward movements were observed. From Penfield and Erickson.¹

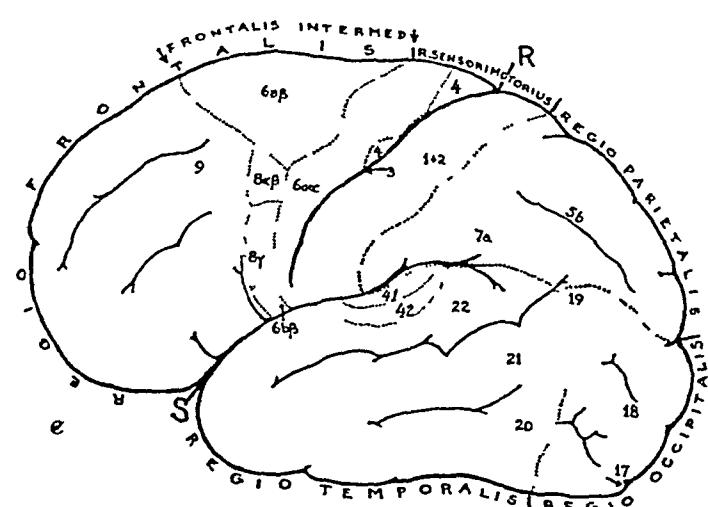


Fig 2.—Surface view of the left motor cortex, slightly tilted to show Vogt's areas α , β and γ . These are the areas for voluntary ocular movements to the right, and possibly upward. From Penfield and Erickson.³

No cortical areas have been discovered where stimulation produces either downward movements or movements of convergence

not individual ocular muscles, are represented in the cortex. With the exception of the muscles

3 Penfield, W., and Erickson, T. C. Epilepsy and Cerebral Localization, Springfield, Ill., Charles C. Thomas, Publisher, 1941, p. 45.

which innervate the lids, there is no isolated representation of any of the ocular muscles in the cortex.

Stimulation of the second frontal convolution in the higher mammals usually produces conjugate deviation of both eyes to the opposite side, but the early experiments of Russell and Sherrington⁴ showed that after section of various groups of the ocular muscles stimulation of the second frontal convolution on one side might lead to conjugate deviation of the eyes in almost any direction, depending on the combination of the muscles which were made ineffective by sectioning, so they concluded that this region was responsible for voluntary ocular movements in all directions, laterally and vertically. They argued that since lateral movements are so much more commonly exercised, these movements overshadow the control of the other conjugated movements. Stimulation of the right frontal convolution usually produces conjugate deviation of the eyes to the left side, and stimulation of the cortex of the left frontal convolution produces deviation of the eyes to the right side. Destruction of either area produces paralysis of conjugate movement of the eyes toward the side of the lesion, without impairing the action of the individual muscles concerned and without producing diplopia, since the limitation of movement affects both eyes equally and simultaneously.

Cortical Centers for Vertical Gaze.—Although all investigators are agreed on the cortical origin of lateral movements, there is no such unanimity on the origin of the movements of vertical gaze. The experiments of Russell and Sherrington⁴ and those of Grünbaum and Sherrington⁵ indicated that upward deviation may be produced by stimulating either frontal area, while Duke-Elder⁶ claimed that stimulation of the upper part of either frontal convolution produces downward movement and stimulation of the lower part produces upward movement of the two eyes.

Since there is often a gradual recovery of function after lesions which completely prevent conjugate deviation of the eyes to one side, it is probable that there is some degree of bilateral innervation for conjugate lateral movements.

Course of Fibers to the Pontile Center.—The fibers which arise from the pyramidal cells of

⁴ Russell and Sherrington, cited by Riley⁷.

⁵ Grünbaum, A. S. F., and Sherrington, C. S. Observations on the Physiology of the Cerebral Cortex of Some of the Higher Apes, Proc Roy Soc London **69** 206, 1901-1902.

⁶ Duke-Elder, W. S. Text-Book of Ophthalmology, St Louis, C. V. Mosby Company, 1933, vol 1, p 207.

the second frontal convolution pass into the corona radiata of the white matter and enter the knee of the internal capsule as part of the pyramidal tract (fig 3). They turn into the internal capsule close to the fibers from the cortical representation of the motor innervation of the face and proceed downward into the pons. Separate contingents of this tract are given off at different levels, the chief of which is that which has to do with vertical gaze, i.e., the fibers innervating the muscles of upward and downward gaze, together with the muscles of the upper eyelid and the frontalis muscle. These fibers leave the pyramidal tract at about the level of the superior corpora quadrigemina, where they probably go to the center for vertical gaze (see page 366).

If there are fibers in this system which have to do with convergence, their presence has never

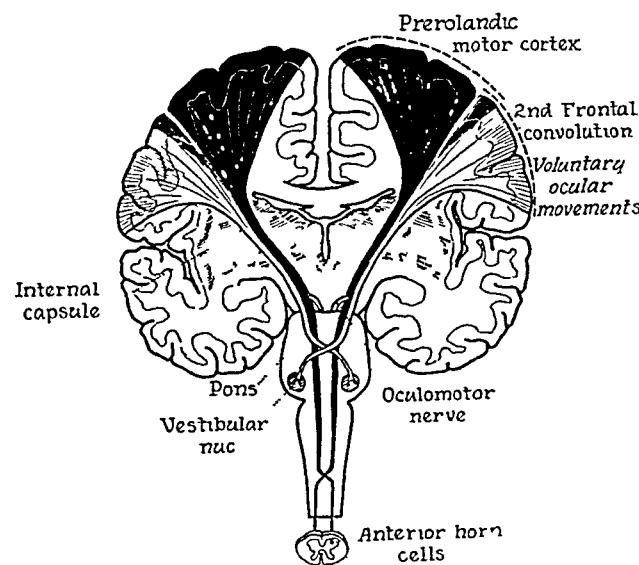


Fig 3.—Diagram of the course of the voluntary oculogyric pathways from the frontal cortex to the pons. The fibers enter the knee of the internal capsule as part of the pyramidal tract. In their course downward separate contingents are given off at different levels, the chief of which is that which concerns vertical gaze.

According to Spiegel and Sommer,⁸ these fibers run into the vestibular nuclei on their way to the hypothetic center for lateral gaze in the pons.

been determined, although convergence movements have been produced by stimulation of the center in the frontal lobe (Riley⁷) and can be initiated voluntarily.

The part of the pyramidal tract which has to do with lateral gaze leaves "the corticonuclear tract as two bundles of fibers, the pes lemniscus superficialis and the pes lemniscus profundus in the midbrain and upper pontile region, respec-

⁷ Riley, H. A. The Central Nervous System Control of the Ocular Movements and the Disturbances of This Mechanism, Arch Ophth **4** 640 (Nov), 885 (Dec) 1930.

tively, descends for a short distance in the mesial fillet and then proceeds dorsally in the tegmentum to the center for lateral movement" (Riley⁷)

Besides conjugate deviation in a horizontal or vertical direction, stimulation of the frontal centers in the lower mammals may produce ocular torsion (Collins and Spiegel⁸) In cats the most frequent result is intorsion of the opposite eye, while the eye on the side stimulated intorts or extorts or does nothing at all No tonic effect of the cortex on torsion could be found, according to these authors and elimination of the cortex and subcortical ganglions in front of the midbrain produced only moderate degrees of torsion Under the influence of anesthetics, however, particularly the so-called brain stem anesthetics, pronounced torsion was observed The range of torsion was from 35 degrees inward to 30 degrees outward There was mostly bilateral intorsion, rarely bilateral extorsion or conjugate deviation

An analysis of this effect of barbiturates showed that it was only partially due to depression of prosencephalic and diencephalic activity and partly to direct action upon the midbrain and upon rhombencephalic supranuclear centers (probably vestibular nuclei)⁹

The Pontile Center —It is generally accepted that the fibers for voluntary lateral gaze cross over to the opposite side of the brain stem just above the level of the sixth nerve nuclei From here their course is not so certain The majority of authors favor the assumption that the fibers end in a pontile center for lateral gaze, although there is no histologic evidence of such a center Its existence is based on the fact that in certain cases in which the nucleus of the sixth nerve is entirely destroyed on one side, there is loss of movement of the homolateral eye outward but retention of the conjugate movement of the opposite eye toward the side of the lesion This proves conclusively that the nucleus of the sixth nerve itself cannot be the center for lateral movement but that either there is a separate center outside the nucleus or the fiber splits before reaching the nucleus of the sixth nerve and sends one part to the homolateral nucleus of the sixth nerve and another to the contralateral nucleus of the internal rectus muscle Most authors have asserted that there is a separate center but that it lies close to the nucleus of the sixth nerve,

(Holmes,¹⁰ Kidd¹⁰), probably in front of the nucleus and nearer the midline This so-called pontile center for lateral gaze receives all of the stimuli which excite horizontal conjugate movements of the eyes, i.e., not only the voluntary impulses previously described but the reflex innervation from the lower visual and auditory systems, proprioceptive impulses from the neck muscles, and impulses from the visuomotor center in the occipital cortex

The Posterior Longitudinal Bundle —From this center the fibers run into the posterior longitudinal bundle, the fiber tract which links up the nuclei of the third, fourth and sixth cranial nerves Spiegel and Sommer¹¹ stated the belief that the corticofugal impulses enter the posterior longitudinal bundle through the mediation of the vestibular nuclei for lesions of these nuclei, as

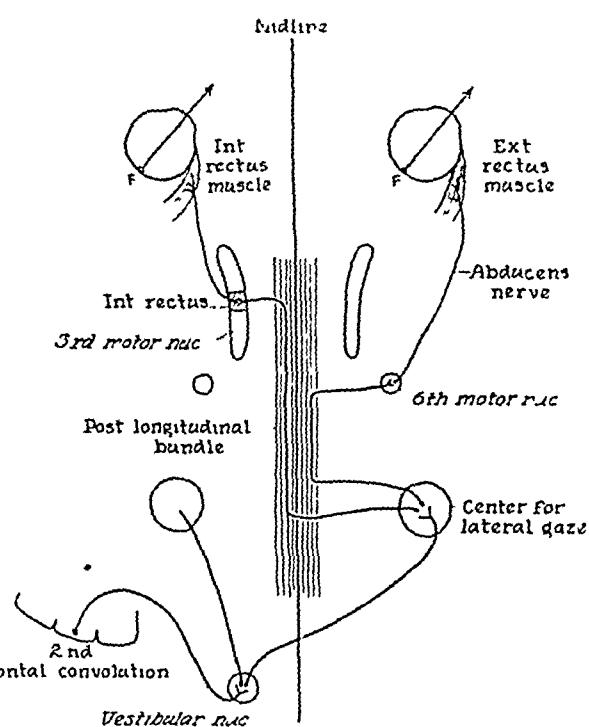


Fig 4.—Diagram of the pathway for voluntary right lateral gaze Starting in the second frontal convolution, the fibers run down in the pyramidal tract to the pons, where they enter the vestibular nuclei, and then to both centers for lateral gaze, near the nuclei of the sixth nerve This pathway links the voluntary impulses for lateral gaze with the involuntary impulses entering through the vestibular nuclei (see fig 14)

well as physiologic changes in the state of their excitability, essentially alter the effect of stimulating the cortical centers for conjugate movements of the eyes (fig 4) This view, according to these authors, explains how the law of reciprocal innervation (inhibition of antagonists during excitation of a muscle or group of muscles) acts on stimulation of the cortical centers It was

⁸ Collins, D. A., and Spiegel E. Ocular Rotation Influence of Anesthetics and Operations on Various Parts of Central Nervous System, Proc Soc Exper Biol & Med 39:100 (Oct) 1938

⁹ Spiegel, E. A., and Sommer, I. Neurology of the Eye, Ear, Nose and Throat, New York, Grune & Stratton, Inc 1944, p 390

¹⁰ Holmes, G. Palsies of Conjugate Ocular Movements, Brit J Ophth 5:241 (June) 1921 Kidd, L. J. Fourth Cranial Nerve, ibid 6:49 (Feb) 1922

¹¹ Spiegel and Sommer,⁹ pp 393-394

shown by Sherrington in experiments on monkeys that one could stimulate the right second frontal convolution and produce conjugate deviation of the eyes to the left even after the muscles which produce levoversion in the left eye have been severed. Under such circumstances, this movement of the left eye outward could occur only by relaxation of the left internal rectus muscle. Cortical stimulation, therefore, not only produces contraction of the ocular muscles which move the eyes conjugately to the opposite side but simultaneously produces relaxation (inhibition) of their antagonistic muscles. This action has been shown to occur also in man.¹² Spiegel pointed out that this action can occur by reason of the fact that the vestibular nuclei act as a relay station which sends fibers into both ipsilateral and contralateral posterior longitudinal bundles.

Once the impulses for horizontal conjugate movements get into the posterior longitudinal bundle, they innervate in an appropriate fashion the nuclei of the ocular muscles necessary to produce the associated movements of the two eyes. Like all voluntary movements, these coarse stimuli must be refined and integrated by reflex activities from all the sources that control the "associated, synergic and voluntary control over the oculomotor movements" (Riley), and these moderating impulses are converged on the neuromuscular apparatus through the medium of this bundle.

Centers for Vertical Gaze—Still less is known of the subcortical centers and pathways controlling voluntary vertical movements of the eyes. The question of the localization of these movements in part of the frontal oculogyric center has already been discussed. Movements of upward and downward gaze must be associated with simultaneous stimulation or inhibition of the muscles which raise and lower the lids. Lesions in the neighborhood of the superior colliculus have long been known to be associated with disturbances in vertical gaze and with changes in the movements or position of the lids, such as ptosis and tucked lids (Collier¹³), so that one can be certain the fibers concerned in these movements lie in this neighborhood. Riley concluded that the superior colliculus was either a relay station in the suprasegmental pathway or a subcortical center, similar to the pontile center for lateral gaze. The impulses presum-

ably get into the posterior longitudinal bundle but, unlike the impulses for lateral gaze, do not, according to Spiegel and Sommer, first run through the vestibular nuclei (fig 5). They also expressed the opinion that these impulses may not even run into the posterior longitudinal bundle. They eventually reach the appropriate nuclei of the muscles which raise and lower the eyes and the eyelids.

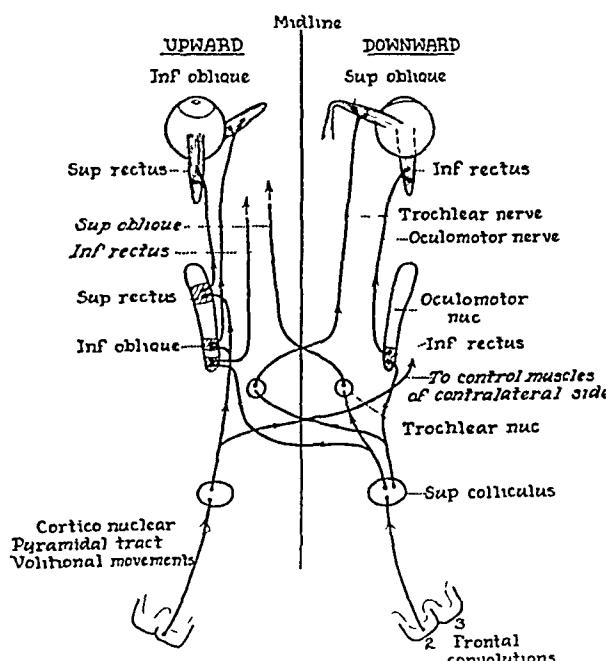


Fig 5.—Diagram of the course of the fibers for vertical gaze. The left half of the diagram shows the course for upward gaze, the right half, that for downward gaze. According to Spiegel and Sommer, the fibers leave the pyramidal tract without entering the vestibular nuclei and run directly to the superior colliculi. From here they are distributed to the appropriate nuclei of the ocular muscles.

Centers and Pathways for Convergence—The cortical center for the willed convergence movements of the eyes is unknown, unless it is the same frontal centers which produce conjugate deviation. There is plenty of evidence to support the belief that there is a subcortical center for convergence, for convergence alone may be paralyzed while the horizontal conjugate movements are retained and vice versa. There must be a special center for convergence, therefore. Biouwer placed this center in Peilia's nucleus, a single nucleus of small cells lying between the paired Edinger-Westphal nuclei, on the basis of his phylogenetic studies (fig 6).

Centers and Pathways for Divergence—There is less evidence of either a cortical or a subcortical center for willed movements in divergence, and this is to be expected since there is no voluntary control of divergence (other than relaxa-

12 Adler, F. H. Reciprocal Innervation of Extraocular Muscles, *Arch Ophth* 3:318 (March) 1930.

13 Collier J. Nuclear Ophthalmoplegia with Special Reference to Retraction of Lids and Ptosis and to Lesions of Posterior Commissure, *Brain* 50:488 (Oct.) 1927.

tion of convergence) in the normal subject. Cases of bilateral willed divergence have never been recorded, and unilateral willed divergence may be brought about in rare cases by the relaxation on one side of the convergence impulse while it is maintained on the opposite side. Such cases do not prove the existence of a divergence center. Some authors, however, postulate the existence of such a center close to the sixth nerve nuclei (Bruce¹⁴). In the majority of cases of divergence paralysis the characteristic symptoms are soon followed by definite paralysis of one or both sixth cranial nerves, so that if a center exists it must lie close to these nuclei.

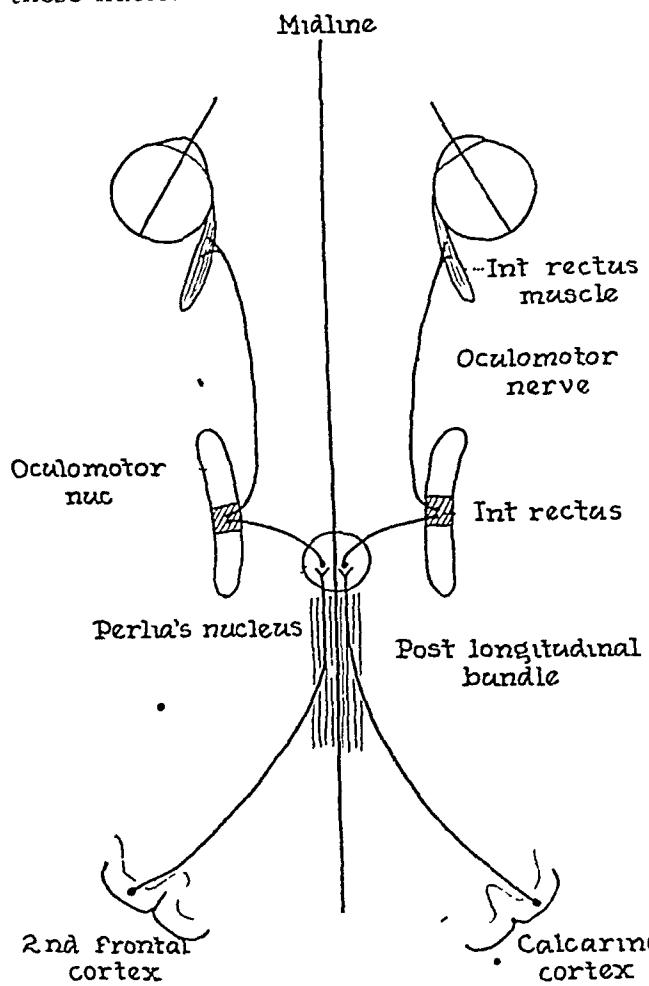


Fig. 6.—Diagram of the course of the fibers for convergence. A hypothetic fiber has been drawn from the second frontal convolution for voluntary convergence, although there is no experimental evidence to indicate the existence of this innervation. There is good evidence for the existence of the involuntary innervation from the occipital cortex, as shown on the right side of the drawing.

Although stimulation of the centers and pathways described in the preceding paragraph results in forced conjugate movements of the eyes these parts of the central nervous system have to do normally only with voluntary, or willed, movements. If through disease or experi-

mental destruction these centers are prevented from working, all the lower reflex movements of the eyes are still kept intact.

In man the importance of the reflex control of the ocular movements far outweighs that of the voluntary control. In nearly all the activities of the eyes the movements are dominated by the reflex control although they may be initiated by a willed effort. The act of reading, for example, consists of a series of finely coordinated horizontal conjugate movements by means of which a certain span of words is fixed by the two maculas for a brief period of time. These shifts in fixation are carried out reflexly, in fact, entirely unconsciously, seven or eight being the usual number in an ordinary line of print. At the end of the line the eyes are moved to the left again by a voluntary effort of which the reader is aware and the visual axes moved down to the next line of print, when the process is repeated all over again. The act of reading would be a painfully slow process if these horizontal shifts had to be made voluntarily.

REFLEX CONTROL OF OCULAR MOVEMENTS

If there are gaps in knowledge concerning the willed ocular movements knowledge regarding the reflex control of ocular muscle tone is still more meager, so that one is in no position today to get a complete picture of this important mechanism controlling the position of the eyes.

All willed movements of the body have to be coordinated and modified to fit in with changes in posture of the body as a whole or of its various parts, otherwise they become ataxic. The great coordinating center for smoothing out muscular activity in time and extent is the cerebellum. In the case of the eyes most of this is accomplished by impulses coming from the vestibular division of the eighth cranial nerve. In addition, there are other sources of tone which will be described, and perhaps many others the existence of which is not yet recognized.

A few examples will show how necessary such a mechanism is for assuring properly controlled movements of the eyes. When the head is in the erect posture, dextroversion of the two eyes in the horizontal plane is carried out mainly by the contraction of the right external rectus and left internal rectus muscles, together with reciprocal inhibition of their antagonists. If the head is tilted on the right shoulder, however, a contraction of these two muscles alone would not effect dextroversion in the plane of the horizon but will turn the eyes obliquely down and to the right. Other muscles must therefore be brought into play to keep the eyes in the same plane of the horizon and to turn them to the

¹⁴ Bruce, G. M. Ocular Divergence. Its Physiology and Pathology. Arch. Ophth. 13: 639 (April) 1935.

right. Hence the position of the head in space must modify profoundly the muscles which must be activated to produce any desired movement of the eyes. To this end the ocular muscles are kept under a constant changing state of tone through the vestibular nuclei by impulses coming in from the neck muscles and from the otolith apparatus in the labyrinths.

Further, when the head is tilted on the shoulder, the eyes are known to execute a torsional movement around their anteroposterior axes, so that as the head tilts the vertical meridians of the corneas stay erect and do not incline with the head. This compensatory torsional movement is brought about by an increase in tonus of those muscles which tend to keep the vertical meridians of the corneas erect, as the

which it seems to come. A painful stimulus applied to the face causes the eyes to turn involuntarily to the place where it is located. Thus the cochlear division of the eighth nerve and the trigeminal nerve exert an influence on ocular muscle tonus, mediated through the posterior longitudinal bundle.

The most important reflex source of tone known, other than the visual, is that mediated by the vestibular division of the eighth nerve. Duke-Elder¹⁵ has given a good description of the neuroanatomic details (fig 7). This complex mechanism serves to correlate changes in posture and movements of the eyes by means of reflexes which, for the sake of study, may be divided into static reflexes, due to changes in position of the head in respect to gravity, and statokinetic reflexes which occur as a result of movement of the head through space.

1. Static reflexes. These reflexes have already been mentioned briefly as altering the muscles called into play to secure any desired change of position of the eyes when the head is tilted on the neck. They arise as proprioceptive impulses from the neck muscles. As the head is tilted on the shoulders the neck muscles of one side are put on a stretch, and this initiates the stretch reflexes, which are known to occur in most skeletal muscles. In the lower mammals the influence of the neck muscles is considerable so that all the muscles of the eyes are under their tonic influence. In man their influence is felt much less, so that a rotation of the head on the trunk of 40 degrees produces a compensatory change in the position of the eyes of only 2 to 3 degrees (Fischer¹⁶).

Of more importance in man than the neck reflexes are the changes in tonus which arise as a result of changes in the position of the otolith organs of the labyrinths. All of the external ocular muscles, with the exception of the external and internal rectus muscles, are under the tonic control of the otolith apparatus, and changes in tilt of the head are compensated for by an effective change in tonus of the muscles which cause ocular torsion. It is the otolith apparatus which acts effectively to keep the vertical meridians of the corneas vertical when the head is tilted on the shoulder.

2. Statokinetic reflexes. Whenever the head is moved in space a movement of the fluid in the semicircular canals is set up which effects changes

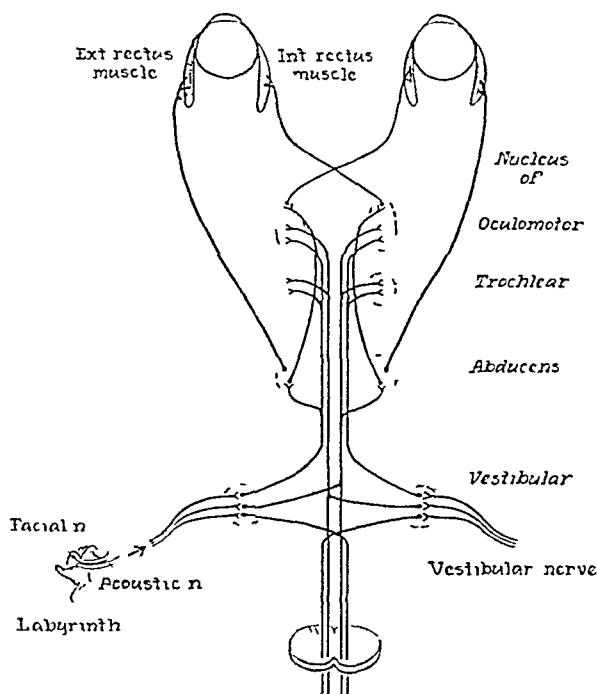


Fig 7.—Diagram of the reflex innervation of the ocular muscles through the vestibular nuclei. From here the fibers enter the posterior longitudinal bundle and are then distributed to the ocular muscles. Tonic impulses from the neck muscles, the otolith apparatus and the semicircular canals are thus sent to the muscles.

head is tilted to the right or to the left. If the head is tilted to the right, for example, levotorsion must be produced in both eyes to keep the vertical meridians vertical. An increase in tone must therefore be sent to the right superior oblique and superior rectus muscles and to the left inferior oblique and inferior rectus muscles. These counterbalancing torsional movements are initiated by the otolith apparatus.

All of the sense organs of the body send impulses into the central nervous system which modify at one time or another the state of tone of the ocular muscles. A sudden loud noise causes the eyes to turn reflexly to the side from

15 Duke-Elder,⁶ p 292.

16 Fischer M H. Messende Untersuchungen über die Gegenrollung der Augen und die Lokalisation der scheinbaren Vertikalen bei seitlicher Neigung (des Kopfes, des Stammes und des Gesamtkörpers) Neigungen bis 40°, Arch f Ophth 118: 633, 1927.

in tone of some of the oculai muscles. The group of muscles affected depends on the semicircular canals which are stimulated, and this, in turn, depends on the posture of the head in respect to gravity during the movement in space. It is quite outside the field of this paper to elaborate on this subject, except to point out that such alterations of tone are constantly acting in the normal subject. The effect of such changes in tone is a conjugate movement of both eyes together laterally or in the vertical direction. It is customary to refer to the direction of nystagmus according to the quick component. If the quick component is to the right, one speaks of the nystagmus as being to the right. However, it is the slow component, in this case to the left, which is the essential part of nystagmus. The slow deviation of the eyes to the left is caused by tonic impulses from the labyrinths, and the quick return from this position is merely a phase of recovery. (The origin of this phase of nystagmus is still the subject of debate.)

Proprioceptive Sense of the Ocular Muscles
—A number of facts suggest the presence of a proprioceptive sense in the ocular muscles which orient and modify certain visual phenomena, such as projection and stereopsis. It is difficult to explain some of the phenomena of paralyses of ocular muscles without assuming some form of proprioception from the paretic muscle. On the other hand, most of the evidence refutes the existence of proprioception in its strictest sense.

In the general musculature of the body it is possible to prove true proprioception by demonstrating the presence of specialized end organs in the muscle, such as the muscle spindle, and by finding special fiber tracts in the central nervous system which carry these impulses set up in the muscle. The muscles with proprioceptive sense also have stretch reflexes, which can be proved physiologically.

In the case of the ocular muscles it has not been possible to demonstrate these various criteria. Irvine¹⁷ found that the muscle spindles were much fewer and of more primitive type than those present in skeletal muscle, and he could not demonstrate the presence of any sensory nerves from the extraocular muscles and tendons. McCouch and Adler¹⁸ were unable to detect any stretch reflexes in decerebrate cats, and Hoffmann¹⁹ failed in the same way in human

beings. There is certainly no anatomic or physiologic proof that proprioceptive sensation is mediated from the ocular muscles. According to Irvine and Ludvigh,²⁰ almost all the facts seem more compatible with the hypothesis of an innervation sense than with that of a proprioceptive sense. From this point of view, muscular activity still forms the basis for the judgment of direction when the eyes are moved, but this "judgment is not founded on the actual contraction of the muscles but upon the 'will' to move them." When the eyes are moved to the right in a dark room, one is conscious of the position they are in not from proprioceptive sensations from the muscles but from the willed effort in turning them.

In support of this hypothesis one can point to the fact that when the eyes are moved reflexly, the subject is quite unconscious of their position—in fact, often of their movement. In the case of nystagmus due to labyrinthine stimuli, whether resulting from disease or artificially induced by rotation in a chair or by douching the ear with cold water, the subject does not know that his eyes are moving but, instead, is conscious only of the apparent movement of the room. Everything around him seems to be turning, while he feels certain that neither his eyes nor the rest of his body is moving. There may, however, be a sensation of falling. The same is true of optokinetic nystagmus. During the movements of the eyes which occur on looking out of a moving railway coach at the passing scenery, the subject experiences no sensation that his eyes are undergoing constant nystagmus. Pulling the eye laterally with forceps gives no sense of its change in position.

Under no conditions in which the eyes are deviated by reflex sources or mechanical pull is the subject aware of that deviation—which he should be if there were proprioception from the ocular muscles themselves—and yet when the eyes are moved by a willed effort, he knows that they have moved and can tell exactly what position they occupy in respect to the orbit.

Penfield and Erickson³ found that sensation of movement of the eyes, although a rare response, resulted from stimulation of the conscious subject in an area of the frontal cortex anterior to the fissure of Rolando in a zone near area 8 (fig. 8). The knowledge of the position of the eyes may be something akin to stereognosis. The elements which are essential for stereognosis are point localization, discrimination of two points and the sense of position and movement (muscle-tendon sense), and these in the case of the hand

17 Irvine, S. R. Histology of Extra-Ocular Muscles. *Arch Ophth* **15**: 847 (May) 1936.

18 McCouch, G. P., and Adler, F. H. Extraocular Reflexes. *Am J Physiol* **100**: 78 (March) 1932.

19 Hoffmann, P. Ist es möglich, die physiologischen Erfahrungen über die Sehnenreflexe (Eigenreflexe) mit den pathologischen in Einklang zu bringen? *Nervenarzt* **2**: 641 (Nov 15) 1929.

20 Irvine, S. R., and Ludvigh, E. J. Is Ocular Proprioceptive Sense Concerned in Vision? *Arch Ophth* **15**: 1037 (June) 1936.

for example, are located in the cortex in the sensory motor region fairly close to the motor representation for the muscles of the hand. It cannot be said that this is evidence either for or against a true proprioceptive sense.

If a patient has recent paresis of an extraocular muscle, for example the right external rectus, he will past point at an object held in the right motor field, even when he uses the right eye only. There are two possible explanations for this past pointing. It may be assumed that in order to turn his paretic right eye out to fix the object he has to contract the muscle more than he normally would, and the proprioception from the muscle therefore gives rise to the sensation that the object is farther to the right than it really is—hence he points to the right, past the object.

On the other hand, Duke-Elder²¹ pointed out that a paretic muscle fails to carry the eye out fully, so that the image falls not on the macula of this eye but on a point slightly to the nasal side of the macula. The fact that the right eye is not turned out far enough is not realized, for there is no real proprioception from the muscle, but only a gross knowledge of the willed effort made in turning the eyes. The image now falls on the nasal side of the macula and hence is projected out farther into the temporal field. Thinking that his eye has actually turned out the whole distance then causes him to past point to the posi-

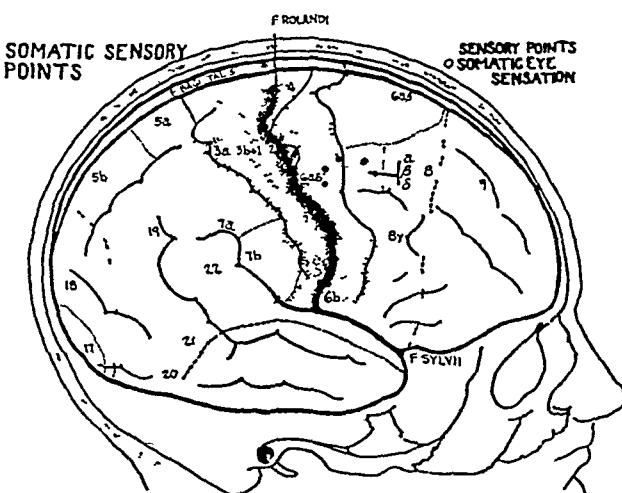


Fig 8.—Diagram of the right motor cortex, showing the points where stimulation in the conscious subject produced a sensation of movement of the eyes. From Penfield and Erickson.³

tion in space which has the local sign of the part of the retina stimulated.

In order to test which of these hypotheses is correct the following experiments were done.

A subject with recent paresis of the right external rectus muscle was seated at a Zeiss perim-

eter, and the left eye was covered. A test spot of light was then placed on the arc of the perimeter in the temporal field 30 degrees from fixation. A black cloth was held in such a way that the subject could not see his own arm while he was asked to point directly to the test spot of light. The difference between the actual position of the spot and the position to which he pointed was then measured. Two test objects were used: a large white spot of light measuring 15 mm and

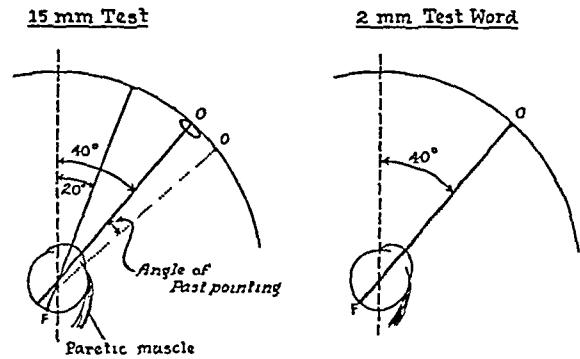


Fig 9.—Right eye of a subject with paresis of the right external rectus muscle. On the arc of a Zeiss perimeter a light, O, has been placed at 40 degrees in the temporal field. With the left eye covered, the subject is requested to look at the object and to point with his right hand to it. The right hand is shielded from his view entirely, so that he is not conscious of where he is pointing. The angle of past pointing is then measured.

On the left the diagram shows that the eye does not turn out to 40 degrees to look at a large test object, i.e., a 15 mm light, but turns out only to 20 degrees, this being sufficient for the subject to see the light. The image therefore falls on the nasal side of the fovea and hence is projected into space at O'. The subject therefore past points to O'.

On the right the diagram shows what happens when a small test light and word are used, of such a nature that in order to see what the word is the eye must be turned out all the way so that the image falls on the fovea. In this case the projection is correct and there is no past pointing.

a small spot of light measuring 2 mm and illuminating a letter or small word. This word was small enough that the subject had to turn the eye all the way out so that its image fell on the fovea before he could read it.

It was found that when the large spot of light was used the angle of past pointing was much larger than when the small spot and letter were used. When the large spot is used, the subject does not have to turn his eye out all the way so that the image falls on the fovea in order to see it, and under these circumstances his past pointing is considerably greater than when he looks at the small spot, which must fall on the fovea (fig 9).

Now if the angle of past pointing depended on false proprioception from the palsied muscle, it would be either the same or greater when the

small spot was used, for the eye has to turn out farther for this test object than for the large test spot. The angle of past pointing is determined by the position of the image on the retina. When this falls on the fovea, as it does when the small spot is used, the projection is good. When the eye is not turned out quite far enough and the image falls on the nasal side of the fovea, as it does when the large test spot is used, the projection is to the right of the object to that part of space which has the local sign of the retinal receptors on which the image falls.

This experiment was done on 2 subjects with recent palsy of the external rectus muscle and on 1 normal subject in whom an injection of procaine hydrochloride along the external rectus muscle produced a paresis of this muscle, with typical limitation of movement and homonymous diplopia for five hours

W R, suspected of having a brain tumor, had paresis of the left external rectus muscle, of three weeks' duration. No other muscles were involved. Central visual acuity was normal. The fields were normal. There were choking of the disks of 1 D and pronounced hypertensive changes in the retinas.

Position of Test Object, in Degrees	Angle of Past Pointing, in Degrees	
	15 Mm Test Spot	2 Mm Test Spot and Word
10	18	2
10	18	0
10	18	0

G McC, had paresis of the right external rectus muscle of two weeks' duration. The condition followed spinal anesthesia for operation on the gallbladder. No other muscles were involved. The eyes were otherwise normal.

Position of Test Object, in Degrees	Angle of Past Pointing, in Degrees	
	15 Mm Test Spot	2 Mm Test Spot and Word
10	8	3
10	5	3
10	5	5

In F H A, a normal subject, paresis of the right external rectus muscle was produced by injection of 2 per cent procaine hydrochloride. The figures given in the tabulation were obtained after typical paresis was produced.

Position of Test Object, in Degrees	Angle of Past Pointing, in Degrees	
	15 Mm Test Spot	2 Mm Test Spot and Word
10	5	0
30	3	2
40	6	3

In the third case measurements taken before the injection of the procaine showed no difference in the angle of projection (there was no past pointing) when the large test spot and the small spot and light were used.

The Visual Fixation Reflex—The most important source of reflex activity in man comes from the visual impulses themselves. The fovea, being the point of greatest visual acuity, must be placed so that the image of an object in space

falls on it in order to be distinctly seen. The voluntary movements of the eyes take care of this when there is a conscious need for foveal vision. But, in addition, nature has further provided that once the image is on the macula it will stay fixed there, reflexly, or if it is near the macula, the eye will be moved reflexly so that the fovea receives the image. This result is attained by an involuntary reflex, called variously the visual fixation reflex, the fusion reflex (when both eyes are so moved that the image falls on each macula), the optomotor reaction, etc. Whenever the image of a moving object tends to move off the macula in one direction, an increase in tonus occurs in those muscles which move the eyes in that direction, thus the eyes are reflexly turned to follow the object (figs. 10, 11 and 12).

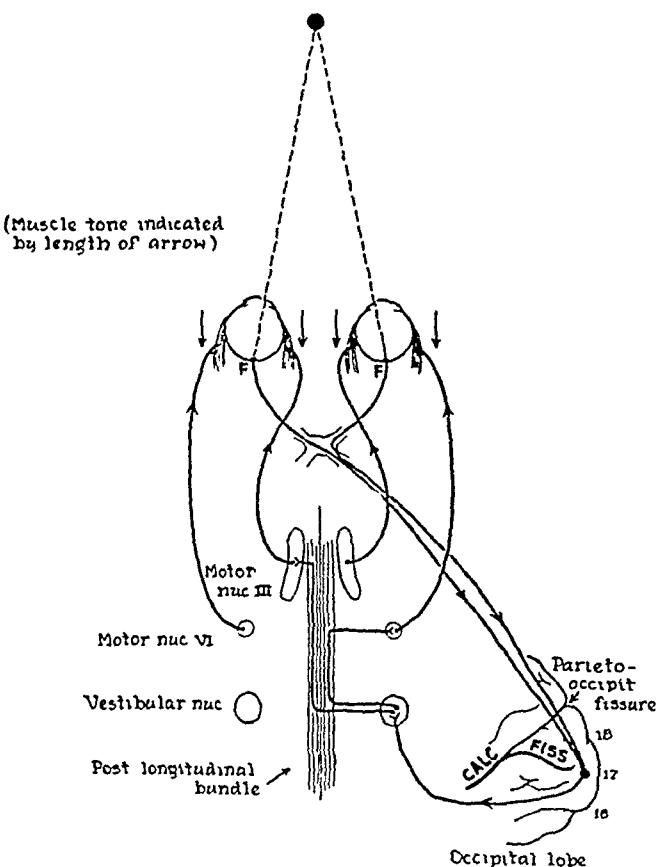


Fig 10.—The image of the dot straight ahead of the eyes falls on the foveas. The impulses are carried up to the extreme tip of the occipital lobe along the calcarine fissure. The optomotor fibers carry impulses from here to the vestibular nuclei, which distribute tone to the ocular muscles (amount of tone indicated by length of arrow in diagram). As long as the images are on the foveas, the tone of the muscles turning the eyes to the right is equal to that of the muscles turning the eyes to the left. The diagram purposely begs the question of the bilateral representation of the foveas. It may be imagined that the same stimuli go to the left calcarine cortex, as is shown here to the right.

This reflex is demonstrated in daily life by watching a person looking out of a railway coach at the surrounding scenery as it passes by the window. The eyes will be found to make a series of movements consisting of a slow phase in the direction the objects seem to be moving and a

rapid phase in the opposite direction. The movements continue as long as the person has his eyes open and pays attention to the scenery. The person may or may not be aware of the fact that his eyes are moving. This is the so-called railroad nystagmus. It can be simulated in the laboratory by having the patient look at black and white stripes on a moving drum. Here it is called optokinetic nystagmus.

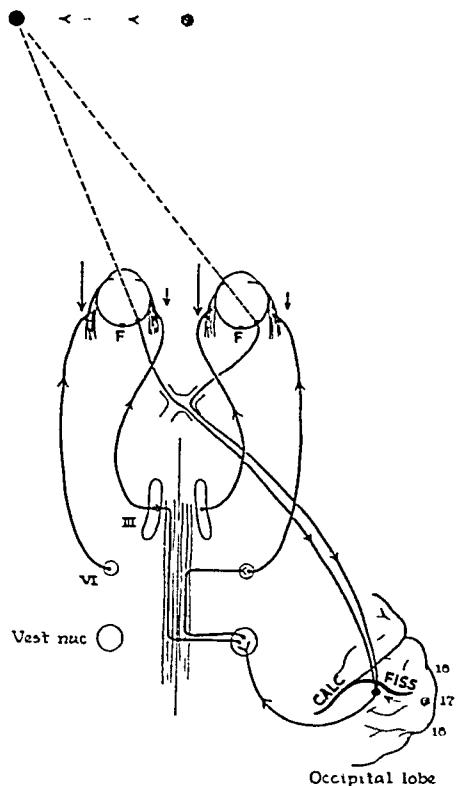


Fig 11.—The spot has moved to the left, and therefore its image has moved off the foveas onto the right halves of the two retinas. The visual impulses are carried up to the occipital cortex, to cells which lie farther forward along the calcarine fissure than those which come from the foveas. From these cells an optomotor impulse is sent to the vestibular nuclei which diminishes the tone of the muscles which turn the eyes to the right and increases the tone of those which turn the eyes to the left. The eyes are therefore turned to the left until the image of the spot once more falls on the foveas.

The same reflex produces involuntary fusional movements of each eye in an effort to maintain binocular single vision when weak prisms are held up in front of one eye while the subject looks at a light at 6 meters. If a weak prism is held up suddenly base-out in front of the right eye, the right eye will quickly and involuntarily turn in to bring the fovea in line again with the object of regard. If the prism is weak, i.e., 1 to 2 prism diopters, the movement will be made without the patient's awareness. If the prism is

stronger, or if more prism is continuously added, the patient will be conscious of a momentary diplopia, as the eye involuntarily makes the effort at fusion. There will come a time finally when the amount of prism added will be too great for the involuntary fusion reflex to overcome. The strength of the prism which breaks up the involuntary fixation reflex is the measure of the reflex fusional capacity.

Beyond this point it is still possible to add more prism base out and secure fusion by a voluntary effort. More and more prism may be added and the patient, after some practice, still finds that he can fuse the two images into one. When the point is reached where this is no longer possible, the strength of the prism used is the measure of the adducting power, or prism adduction. Since the patient soon learns that he can increase his convergence power by calling on his accommodation,

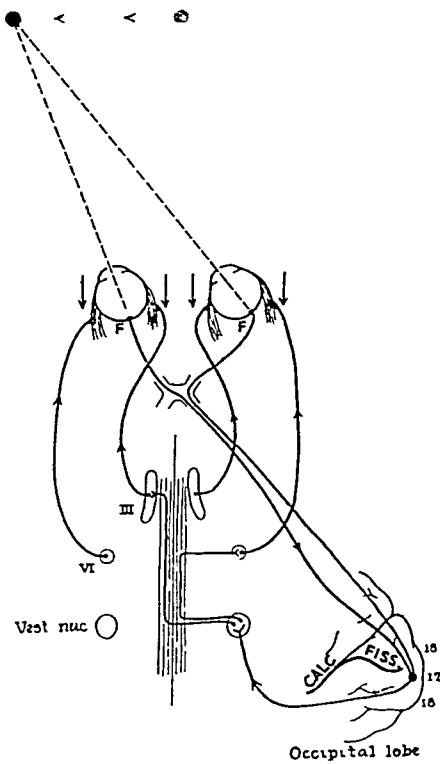


Fig 12.—The eyes have been turned to the left by means of the visual fixation reflex to follow the movement of the spot. The images which now fall on the foveas again send their impulses up to the foveal localization in the occipital cortex, and the optomotor impulses once again equalize the tone of the muscles turning the eyes to the right and of those turning the eyes to the left, so that the eyes remain fixed as long as the image of the spot remains stationary.

he quickly learns to converge and accommodate as though he were looking at a near object. This presents him with a dilemma. He can fuse the

distant double images of the light by converging and accommodating, but in using his accommodation he obtains blurred images. The trick then, he soon finds out, is to keep together, i.e., to fuse, two images into a single blurred image. That this has been called the adduction power, and thought of by some as representing the strength of a subject's muscles of convergence is testimony to the

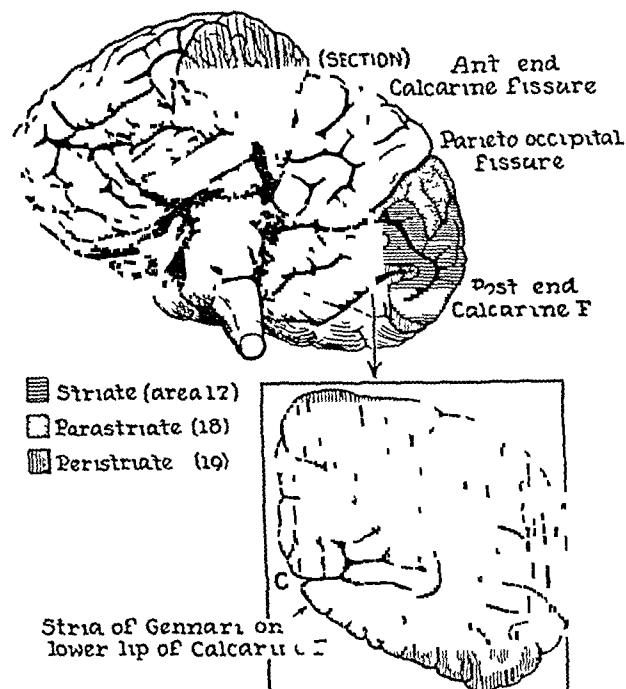


Fig. 13.—Diagram of the mesial half of the right occipital cortex, the left occipital lobe having been cut off. The insert shows a transverse section through the calcarine fissure at the level of the arrow. At this level the parieto-occipital fissure joins the calcarine fissure, so that only the lower lip of the calcarine fissure has the white line of Gennari. Some investigators believe that the cells giving rise to the optomotor impulses of the visual fixation reflex arise in the striate area (area 17 of Brodmann), but according to Hines²³ they originate in the cells of areas 18 and 19 of Brodmann.

naivete of the examiner. After prisms are prescribed for home use, the patient returns with marked improvement in his ability to overcome prisms base out. He has, therefore, according to such an unwitting physician increased the power of his internal rectus muscles, when all that he has done is to learn to dissociate convergence from accommodation, or to accept fused blurred images rather than double clear ones.

The visual fixation reflex is composed of an afferent and an efferent pathway. The afferent pathway²² is the visual pathway, running from the cones of the fovea through the lateral geniculate body and ending in the cells of the calcarine cortex (fig. 13). There is no general agreement however, in which layer of cells of the visual

cortex the motor fibers begin. Most authors consider the cells of area 17 of Brodmann as the beginning of the efferent arc, but Hines²³ gave evidence for believing that the optomotor pathway begins in the cells of layer 18, the parastriate area, and layer 19, the peristriate area, rather than in the striate area itself, or layer 17.

From this optomotor center fibers run into the posterior longitudinal bundle. Their exact pathway is unknown, but Spiegel and Sommer²⁴ have traced them as follows:

Starting from the optomotor zone surrounding the area striata, the fibers seem to pass under the angular gyrus and are observed in "the lateral wall of the posterior and of the inferior horn of the lateral ventricle, internal to the corticopetal optic fibers, in the internal sagittal striatum. Farther on they are found partly in the pretectal area and in the roof of the anterior corpora quadrigemina and in the lateral geniculate body, some fibers could also be traced by the degenera-

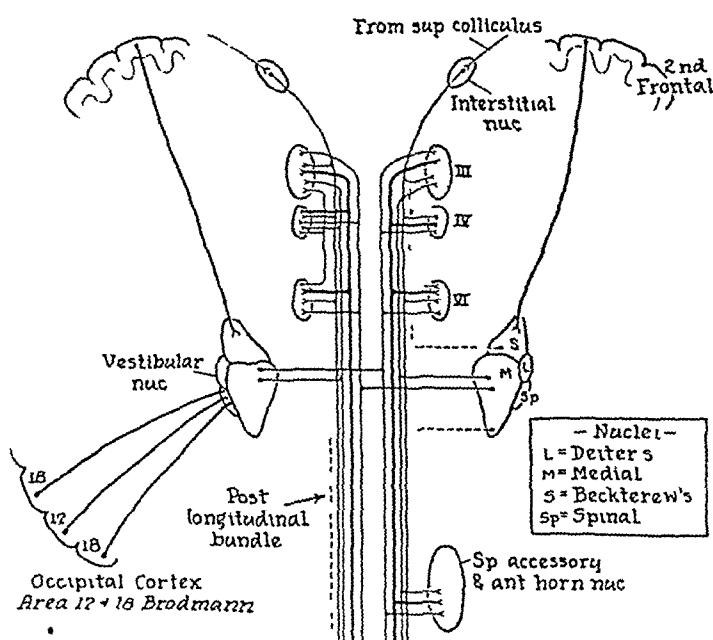


Fig. 14.—Diagram of the posterior longitudinal bundle, showing the voluntary motor innervation of the ocular muscles on the right side and the reflex innervation from the occipital lobes on the left side. It is not intended to indicate that the fibers end in one or another of the vestibular nuclei, as the exact course of these fibers is unknown. The drawing shows a fiber ending in a certain nucleus, e.g., Deiters', merely for convenience.

22 An excellent review of the central visual pathway is that of Kronfeld, P. C. Central Visual Pathway, Arch Ophth 2709 (Dec) 1929.

23 Hines, M. Recent Contributions to Localization of Vision in Central Nervous System, Arch Ophth. 28 913 (Nov) 1942.

24 Spiegel and Sommer,⁹ pp 391-392.

tion method to the basis pedunculi, reaching the pontine nuclei (Barris). From the rhombencephalon on, the course of the oculogyric tract seems to be common with that for the vestibular reflexes to the eyes, in other words the corticofugal impulses apparently use the path of the vestibulo-ocular reflex to reach the eye muscles [fig 14].²⁵ The impulses reach the appropriate ocular muscles through the posterior longitudinal bundle.

Ter Braak²⁵ divided optokinetic nystagmus into two kinds. The first requires the factor of attention, and the second seems to be independent of the frontal cortical centers and, in fact, may be elicited in animals after extirpation of the cerebral hemispheres, this he refers to as the subcortical or passive type.

Accommodation Reflex.—Reference has already been made to the effect of an abnormal amount of accommodation, resulting in excessive convergence and thus giving rise to accommodative convergent squint. There is developed normally a close reflex association between accommodation and convergence, this link is not rigid, but somewhat elastic. By orthoptic training it is possible to make this linkage less rigid, so that a hyperopic person may retain the necessary accommodation to focus on distant objects, yet relax the amount of convergence that would ordinarily be associated with it and thus retain parallelism of his visual axes.

ORTHOPHORIA AND HETEROPHORIA

The anatomic basis for the voluntary and reflex control of ocular movements has been outlined in so far as it is known at the present time. In the normal adult this mechanism keeps the two eyes associated with one another in all directions of gaze, so that the two foveas receive the images of the object of regard. The ocular muscles are under many sources of tone, which are acting constantly and varying among themselves according to the needs of the moment. Even when the eyes are in the primary position and are not being moved, they are kept there by a constant source of tone to the appropriate muscles. This position must not be thought of as one of rest, therefore.

The position of absolute rest is that assumed when the eyes are freed from every source of tone, a condition which occurs only with very deep anesthesia, coma or death. Under these conditions the eyes assume the anatomic position of rest, which is divergence of each eye about 10

degrees, and usually sursumvergence of about 5 degrees. During the waking hours the eyes are never in a position of rest.

It is possible to eliminate some of the sources of tone to the ocular muscles and to determine the position the eyes assume under these conditions. Only the visual sources of tonus can be eliminated readily. If, for example, the subject relaxes his attention and, as one says, lets his thoughts wander from the objects surrounding him, the position of the eyes may change. In some people they diverge greatly. If the image of one eye is made poorer than that of the other by placing smoked glasses of increasing density in front of it, a point will be reached where binocular vision is no longer possible, and the eyes, freed from the fusional impulses of the fixation reflex will take up that position dictated by the remaining sources of tone, whatever they may be.

Whenever the vision of one eye interferes with the use of the two eyes together, an attempt is made by the body to free the eyes from this embarrassment, and the new position which the eyes assume will be that which best eliminates the confusion. This new position may not be the same as that assumed when the eyes are free of the fusional impulses, and therefore dictated by the other, remaining sources of tone, as previously described, but may be a forced position due to new sources of tone from the occipital cortex for the purpose of getting rid of diplopia. The body finds that when the two images cannot be fused together, they can be separated by deviating the eyes from one another, and that this separation helps to avoid the confusion for one of the images may now be suppressed more easily and so the visual axes are turned either in or out to separate the images.

It has become customary to measure the position of the two eyes when the visual fusional impulses are either totally or partially removed and to term this the patient's phoria. If, under these conditions, the visual axes remain so that the image of the object of regard still falls on the two foveas, orthophoria is said to be present. On the other hand, if the images do not fall on the two foveas, heterophoria is said to be present, and the character and degree of the deviation are then determined and measured. It is unfortunate that the implication has arisen that orthophoria is the normal condition and heterophoria an abnormal one, for this is not true. By such standards there are no normal people. It is true that some people are orthophoric for distance when measured by the usual test of the Maddox rod or even the cover test but these are few, the

²⁵ ter Braak, J. W. G. Untersuchungen über optokinetischen Nystagmus, Arch. neerl. de physiol. **21**, 309, 1936.

majority showing 1 or 2 degrees of esophoria or exophoria. When the Maddox rod test is applied, or when the cover test is used, however, almost no one will show orthophoria for near vision. If the Maddox rod test for near vision is conducted in a lighted room, particularly if the patient is asked to measure his own deviation on a scale, such as the Thorington test for near vision, there may be orthophoria due to the stimulus of accommodation, but the examiner has retained under these conditions a part of the visual fusional stimuli he originally sought to eliminate.

The various methods used to dissociate the two eyes will give different measurements, the amounts depending on the extent to which they eliminate the visual fusional stimuli. Heterophoria determined with the Maddox rod tells the effectiveness of dissimilar retinal images in holding the eyes straight as compared with the effectiveness of similar images. (The test should be performed in a dark room, so that there is no influence from the surroundings.)

Heterophoria determined with the cover test tells how effective monocular retinal stimulation is as compared with stimulation of the two retinas simultaneously. Vertical prisms used to determine the lateral phorias show what the eyes will do when they are presented with artificially produced double images which, although similar, cannot easily be fused, the results here are surely not the measure of a fusion-free position, but are most likely that of some forced position which the eyes assume in order best to avoid the confusion of the double images, measurements taken with this method are usually smaller than those with either the Maddox rod or the cover test.

Unfortunately, one does not know exactly what all the other sources of tone are which, combined, give the new position of the eyes freed from all visual fusional impulses. Some of them have already been enumerated, but it is likely that there are others as yet unknown. At present none of them can be eliminated experimentally in human beings.

Two conditions have been studied recently which may throw light on these involuntary mechanisms. These are the effects of alcohol and of anoxemia.

It is commonly supposed that the diplopia which, unfortunately, occurs when alcohol is taken to excess is due to the release of the eyes from visual fusional impulses, similar to the numbing of all the senses. Any heterophoria which was present before the alcohol was taken would then become manifest, if a person had an esophoria before he drank, he would have an

esotropia while under the influence of alcohol, and if he had an exophoria before drinking, he would have an exotropia afterward. This has been shown to be incorrect by a number of investigators.

Powell²⁶ demonstrated that a definite tendency toward esophoria always developed in a series of men and women when given alcohol. This change was constant, gradual and progressive. It was recovered from in about ten hours, and the muscle balance returned to its previous level. It made no difference whether the person was esophoric or exophoric before the alcohol was given, the change was always in the direction of esophoria. The muscle balance for near vision changed in the direction of progressive exophoria. The angle of convergence (convergence near point) showed a progressive decrease, while the prism divergence was not determined.

Powell explained the progressive esophoria at 6 meters on the basis of a weakening of the external rectus muscles and, in defense of this, called attention to the fact that the abducens nerve is termed the weaking of the cranial contents. He explained the decrease in convergence power on the basis of diminished tone and control of the internal rectus muscles.

In 1940 Colson²⁷ repeated these experiments by giving 21 normal adults 2 ounces (39 cc) of rye or scotch whisky every half-hour and testing their muscle balance and voluntary ductions for distance. He found a gradually increasing esophoria in every case, which in 2 instances reached the stage of strabismus with diplopia. The minimum change was 2 prism diopters, the maximum was 11 prism diopters. It made no difference what the original muscle balance was before the alcohol was taken.

Duction tests showed that according to the usual notation the abduction was reduced in every case, but if allowance was made for the state of the muscle balance, there was no change in the abduction. The real adduction was decreased in every case, but in the figures the author gives this decrease is not striking. Both the conventional and the real adduction were hardly changed at all in 2 cases and were only greatly reduced in 1 case, and these were the only ones in which measurements were made. From this observation one could hardly draw any conclusions regarding duction power.

²⁶ Powell, W. H., Jr. Ocular Manifestations of Alcohol and Consideration of Individual Variations in Seven Cases Studied, *J. Aviation Med.* 9:97 (June) 1938.

²⁷ Colson, Z. W. Effect of Alcohol on Vision, *J. A. M. A.* 115:1525 (Nov 2) 1940.

From these experiments it cannot be determined how alcohol produces esophoria for distance. One might guess that it produces its effect by stimulation of the convergence center. The production of torsional movements in cats under the influence of barbiturates has already been mentioned. The mechanism may, of course, be the release of inhibition from higher centers on the convergence center, so that too great an innervation to the internal rectus muscles is set free. It may be a weakening of the divergence mechanism. Further pharmacologic investigation is needed before it can be ascertained where alcohol acts.

The eyes act in a similar way under the influence of severe anoxemia. Although Wilmer and Berens²⁸ found that anoxia produced in a low pressure chamber resulted in an increase of any preexisting heterophoria, Velhagen²⁹ reported the same kind of changes as those which occur in acute alcoholism, i.e., a pronounced development of esophoria. No matter what the subject's muscle balance was to start with, according to this author, the change is always in the direction of esophoria as the atmospheric pressure is reduced. At 3,000 meters his results were not conclusive, but at 5,000 to 6,000 meters the increase in esophoria was considerable. At the near point there was a change similar to that with alcohol, i.e., a tendency toward increasing exophoria. Velhagen spoke of this as a convergence insufficiency. Curiously, he suggested that the changes he observed were probably due to alterations in the muscles themselves, as a result of changed metabolism due to the anoxemia, since he was unable to satisfy himself that there was any increase in convergence tone or hyperexcitability of the convergence center.

I have repeated these experiments on the effects of anoxia and have been able to verify and further to amplify Velhagen's results. These investigations will be reported on later in the ARCHIVES. It was found that during oxygen lack all subjects become more esophoric whether they were esophoric or exophoric to start with. There was no constant change in their muscle balance for near vision. During oxygen lack there was a shift in the range of fusion toward the convergent position, but the range itself showed little variation from normal. This would indicate that during anoxia the convergence center is either released from inhibition or is directly stimulated.

²⁸ Wilmer, W. H., and Berens, C., Jr. The Effect of Altitude on Ocular Functions, J. A. M. A. **71**: 1394 (Oct 26) 1918.

²⁹ Velhagen, K., Jr. Heterophorie unter den Bedingungen des Hohenfluges. Luftfahrtmedizin **1**: 344, 1937.

COMMENT

The following should be considered possible sources of abnormal convergence tone:

Proprioception from the Ocular Muscles—If true proprioceptive impulses originated in the ocular muscles, as in other skeletal muscles, a theory of strabismus might be conceived on the basis of abnormal proprioception. All the evidence points to a different mechanism, however, and one is forced to the conclusion that the body obtains information of the position of the eyes in respect to the orbits from the pathways of willed innervation, and not from the muscles directly.

There are grounds for believing that the position of the eyes in the orbits influences the sensory response, however. It has frequently been noted that patients who have divergent strabismus with equal vision in the two eyes and who ordinarily alternate cannot be made to see binocularly through one of the major stereoscopes even when the tubes are placed at the angle of squint. As soon as the eyes are straightened by operation, however, they see binocularly, some have first or second degree fusion, and still others stereopsis. A plausible explanation would seem to be that binocular vision is possible only when the eyes are in the natural position in respect to each other in the orbits, and that when they are divergent, owing to faulty innervation of the ocular muscles, binocular vision is inhibited—even though the images are presented to the two eyes along the visual line of each.

Cortical Centers for Convergence—If there are cortical centers for voluntary convergence, which there probably are, their location is unknown at present. The occipital centers for the visual fixation reflex must give rise to convergence tone in keeping the foveas fixed on an object either approaching or receding from the eyes. There is as yet no evidence which could incriminate this mechanism. I have examined a number of children with strabismus to see whether their optokinetic nystagmus differed from that of normal children, and the results so far are negative. The movements have not been photographed as yet, however, and no conclusions can be drawn. Other methods of investigating the fusional fixation reflex should be devised, as this is an attractive possibility to be explored.

Subcortical Centers and Pathways for Convergence and Divergence—Under conditions of acute intoxication with alcohol or as a result of severe anoxia, the visual axes become convergent and an esophoria frequently becomes an esotropia. Unfortunately, it is not yet known what causes this—whether there is a stimulation of the convergence center or a release of this center from

cortical inhibition or a paralysis of the divergence mechanism. It is likely that either the first or the second possibility is the true cause. If the change were due to a paralysis of divergence, why is it that during sleep or anesthesia the position is that of divergence? It seems more probable that the convergent position is due to hyperactive tonic impulses sent to the internal rectus muscles.

There is too little evidence for one to do more than suggest that the type of convergent squint under discussion might be caused by a similar mechanism in the growing infant. But it is not improbable. There can be no doubt that comitant squint is due to an abnormal supranuclear source of tonus, for by its very nature the angle of squint remains the same in all positions of gaze. (For an excellent discussion of comitance see Chavasse²) It can be readily seen that in the infant if the eyes were forced into the convergent position from a hyperexcitable convergence center the result would be just what it is—one eye would take up fixation instead of both eyes remaining convergent while the other eye would assume the whole of the angle of convergence. The result would be a fixing eye and a squinting eye and if the two eyes were of equal value (same refractive error and acuity of vision), the squint would be an alternating one. When one eye took up fixation, the whole burden of the overconvergence would be on the fellow eye. If one eye were better than the other (greater refractive error or some other obstacle to vision), then it would remain the fixing eye, and a monocular squint would develop.

Vestibular Apparatus.—Impulses reaching the posterior longitudinal bundle through the vestibular nuclei are of considerable importance in regulating the tone of the ocular muscles. Vestibular impulses cause conjugate movements of the eyes laterally and vertically, and in man these movements are always equal. Bartels³ found in rabbits that stimulation of one labyrinth affected the tone of the muscles of the ipsilateral eye more than of the opposite eye, but these results do not apply to man. Besides, it has never

30 Bartels, M. I. Ueber Regulierung der Augenstellung durch den Ohrapparat, *Arch f Ophth* **76** 1, 1910, II Schielen und Ohrapparat, *ibid* **77** 531, 1910, III Kurven des Spannungszustandes einzelner Augenmuskeln durch Ohrreflexe *ibid* **78** 129, 1911, IV Die starker Wirkung eines Ohrapparates auf das benachbarte Auge, *ibid* **80** 207, 1911.

been shown that vestibular tone has anything to do with convergence. This seems to be the only associated movement of the eyes which is not affected by changes in vestibular tone, and one can hardly imagine, therefore, that squint is produced by an abnormality of this mechanism.

Sommer¹ examined a large series of normal persons, patients with high esophorias and patients with convergent squint and found no effect of caloric stimulation of the vestibular apparatus on the phoria or the angle of squint. In cases of so-called oblique strabismus, in which the squinting eye turned upward on adduction and downward on abduction, Ohm³² claimed to have demonstrated a vestibular component, but the evidence presented is not convincing.

CONCLUSIONS

In all cases of convergent squint, except those in which the condition is due to paralysis of an ocular muscle, the fundamental cause is an abnormal convergence innervation. There is no difference between an esophoria and an esotropia save that in the former the eyes are still held together by the visual fusional stimuli whereas in the latter this mechanism has failed to maintain fusion. Regardless of the state of perfection of fusion, the important factor in the causation of squint is the force which produces it, and that is an excessive convergence innervation.

In the case of accommodative squints one does not have far to look for the origin of the excessive convergence, and Donders' theory for this condition is as correct today as it was when he formulated it. There are many squints, however, which are not of this origin, and in these one must look elsewhere for the source of, and the reason for, the excessive convergence. From a review of the physiologic mechanisms concerned in normal ocular movements, one can find possible sites of interference which could lead to comitant squint, but as yet the evidence is merely suggestive. It is sufficient, however, to warrant further research, free from the bias of any preconceived theory.

Hospital of the University of Pennsylvania

31 Sommer, I. Labyrinth und Schielen, *Ztschr f Augenh* **65** 14 (May) 1928

32 Ohm, J. Schragschielen, *Arch f Augenh* **99**, 619 (Nov.) 1928

USE OF METHYL CELLULOSE IN OPHTHALMOLOGY

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PORTLAND, ORE

There has been need in ophthalmology for a nonirritating and chemically inert colloid which would dissolve in water to produce a viscous, colorless solution having a high degree of transparency and a refractive index similar to that of the cornea. Such a solution would be useful as a bland vehicle for ophthalmic medicaments, as a substitute for natural secretions in cases of keratoconjunctivitis sicca and as an emollient and cohesive solution to be used with contact lenses and gonioscopic prisms. Attempts have been made to adapt various compounds for these purposes, with only partial success. Acacia, tragacanth and gelatin have been most widely used, but they are chemically unstable, have high refractive indexes and are good mediums for the growth of bacteria and fungi. A synthetic substance methyl cellulose,¹ has considerable advantages over these naturally occurring gums. Its properties and some of its ophthalmic uses are reported here.

Methyl cellulose is a water-soluble cellulose ether with a high degree of purity and uniformity. It is produced in six types, graded according to the degree of viscosity. For ophthalmic purposes the highest viscosity type (4,000 centipoises) is preferable, as only a small quantity need be added to aqueous solutions to increase the viscosity greatly without significantly altering its optical properties. Two per cent aqueous solutions have a viscosity many times that of water, but are highly transparent and colorless and have a low dispersion power and a refractive index (1.336) similar to that of distilled water (1.334). In addition, solutions of methyl cellulose are neutral, odorless, tasteless and nearly inert chemically. They are stable in the pH range which is tolerated by the eye and seem unaffected by light or aging. Boiling produces coagulation, but on cooling, methyl cellulose redissolves. Therefore solutions may be sterilized by boiling. Aqueous solutions may be diluted

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This investigation is part of a study being conducted under a grant from the John and Mary R. Markle Foundation.

¹ The preparation used was methocel (Dow Chemical Company).

with ethyl alcohol and are compatible with the drugs commonly used in ophthalmology. Solutions containing only pure methyl cellulose do not support bacterial or fungal growth.

It is recommended that solutions of methyl cellulose be prepared by first mixing the dry material thoroughly with approximately half the required volume of water at boiling temperature and allowing it to soak from twenty to thirty minutes, with agitation. This procedure hastens wetting of the methyl cellulose. The solution does not become clear until the remaining amount of water is added and the mixture cooled to room temperature. Solutions of maximum clarity may be obtained by reducing the temperature to 5 or 10°C during the cooling period and stirring until smooth. Undissolved fibers may be removed by centrifugation.

When used as a vehicle for ophthalmic drugs, a 0.5 to 1 per cent solution of the 4,000 centipoise type of methyl cellulose may be instilled with a small bore dropper, but higher concentrations are more satisfactorily administered in collapsible tubes with small tips. The emollient properties of the colloid reduce irritation of the conjunctiva produced by drugs. Unlike the commonly used oily vehicles of high viscosity, methyl cellulose solutions mix well with secretions and spread smoothly throughout the conjunctival sac. Also, vehicles containing methyl cellulose remain longer in the conjunctival sac than simple aqueous solutions and therefore result in more effective absorption of many ophthalmic drugs, however, highly surface-active compounds, such as tetracaine and dibutoline sulfate (dibutylcarbamate of dimethylethyl-β-hydroxyethyl ammonium sulfate) are adsorbed by the colloid, so that their penetration of the tissues is retarded. Methyl cellulose is best suited to form stable, nonoily suspensions of slightly water-soluble substances, such as sulfamerazine. For example, 1 to 4 Gm of finely powdered sulfamerazine stirred into 2 per cent solution of methyl cellulose in distilled water forms a non-irritating and highly effective unguentum for local treatment of external inflammations of the eye. The drug has a higher affinity for the tissues than for this vehicle, consequently, therapeutically effective concentrations in the con-

junctiva and cornea are readily obtained. Chemical analyses² of normal conjunctiva excised from 3 volunteers one-half hour after a single instillation of 3 per cent sulfamerazine in a 2 per cent aqueous solution of methyl cellulose revealed an average concentration of sulfamerazine of 42 mg per hundred grams in the specimens from the lower fornix and 18 mg per hundred grams in the specimens from the extreme upper fornix.

Solutions of methyl cellulose have cohesive and emollient properties which, along with a neutral reaction, a high degree of clarity and a refractive index similar to that of the cornea, make them superior to simple aqueous solutions for use with contact lenses. Methyl cellulose solutions may be buffered to the alkaline levels usually desired for use with contact lenses, but the first 3 patients to use the solution have found buffering unnecessary. The viscous methyl cellulose solution adheres to the lens and therefore permits the contact lens to be applied to the eye with much less chance of the solution spilling and being replaced by air bubbles than if a simple aqueous solution is used. Also, methyl cellulose solutions have a lubricating action similar to normal conjunctival mucus, so that patients are able to wear the lenses more comfortably and for longer periods when methyl cellulose is added to the aqueous solution. A concentration of 0.5 to 1 per cent of the 4,000 centipoise type of methyl cellulose dissolved in 0.9 to 1.2 per cent sodium chloride is most satisfactory for use with contact lenses. Bubbles accidentally stirred into solutions containing up to 1 per cent methyl cellulose will rise to the surface but will be retained in solutions of higher viscosity.

Methyl cellulose solutions increase the practicability of contact lenses applied for gonioscopy or for examination of the fundus with the corneal curvature neutralized. These solutions are particularly suitable for use with gonioscopic lenses, such as the type recently developed by Allen.³ In this type of lens the water chamber is eliminated and the lens is held in apposition with the cornea by capillary attraction. A highly cohesive film is obtained by moistening the surface of the lens before application with isotonic solution of sodium chloride containing 1 per cent methyl cellulose. The lubricating and emollient properties of the colloid permit prolonged application of the contact lens without damage to the delicate corneal epithelium. The Allen goni-

scopic lenses have been made of a plastic material with the same refractive index as the cornea and the methyl cellulose solutions, so that apparently perfect optical continuity is obtained.

A 0.5 per cent solution of the 4,000 centipoise type of methyl cellulose containing 0.9 to 1.25 per cent sodium chloride has provided an excellent substitute for deficient conjunctival secretions in 2 patients with keratoconjunctivitis sicca. In both patients a superficial punctate disturbance was evident on biomicroscopic examination with the slit lamp, and Schirmer's test was positive before treatment was undertaken. The corneas became clear, and subjective symptoms were relieved by instillations of the methyl cellulose solution at two to three hour intervals. Buffering of the solution was unnecessary. The only complaints referable to use of the colloid were that immediately after instillation it produced an unpleasant sensation of the lids being stuck together. Also, excesses of the colloid would dry on the lashes, but the fine fiber could be removed easily with a damp cloth.

No cases of hypersensitivity to methyl cellulose were noted among the approximately 100 patients who received instillations of this colloid. Also, Hueper, Martin and Thompson⁴ were unable to produce hypersensitivity to the colloid with repeated intravenous injections in dogs.

Deichmann and Witherup⁵ found that the orally ingested methyl cellulose could be completely recovered in the feces, and Hare and Clark⁶ observed that the colloid was not absorbed from closed subcutaneous wounds. Likewise, methyl cellulose did not appear to be absorbed from the conjunctival sac. Weighed quantities of the colloid sealed into the conjunctival sac of rabbits by suturing of the lids and closing of the lacrimal passages were completely recovered after several hours.

Instillations of 1 per cent solution of methyl cellulose into the conjunctival sac of rabbits were made two to three times daily for three months. No evidence of injury to the ocular tissue was found by either biomicroscopic examination with the slit lamp or histologic methods. Practically no inflammatory reaction resulted from the subconjunctival injection of 0.1 cc of a 1 per cent solution of methyl cellulose in albino rabbits.

⁴ Hueper, W. C., Martin, G. J., and Thompson, M. R. Methyl Cellulose Solution as a Plasma Substitute, *Am. J. Surg.* **56**, 629 (June) 1942.

⁵ Deichmann, W., and Witherup, S. Observations on the Ingestion of Methyl Cellulose and Ethyl Cellulose by Rats, *J. Lab. & Clin. Med.* **28**, 1725 (Nov.) 1943.

⁶ Hare, R., and Clark, E. N. Use of Plastic Vehicles for Applying Sulfonamide Compounds to Wounds, *War Med.* **4**, 140 (Aug.) 1943.

² Sulfamerazine—Chemical Reagent, Brochure P. H. 689, Philadelphia, Sharp & Dohme, Inc., 1943.

³ Allen, L. A New Contact Lens for Viewing the Angle of the Anterior Chamber of the Eye, *Science* **99**, 186 (March 3) 1944.

but similar injections into the anterior chamber produced mild endocyclitis. This finding is in accordance with the observation of Hare and Clark⁶ that in closed wounds methyl cellulose creates a foreign body reaction. It would appear, then, that the use of methyl cellulose in the conjunctival sac is a safe procedure except in instances of open wounds leading into the eyeball.

SUMMARY

Methyl cellulose is a synthetic colloid with a high degree of purity and uniformity. In cold water, it forms colorless stable, neutral viscous

solutions with a high degree of clarity, low dispersive power and a refractive index similar to that of the cornea. In the conjunctival sac these solutions mix well with the conjunctival secretions and have an emollient action. Preliminary clinical investigations indicate that methyl cellulose is superior to naturally occurring gums or oils as a vehicle for many ophthalmic drugs as a substitute for normal secretions in cases of keratoconjunctivitis sicca and as an emollient and cohesive medium for use with contact lenses and gonioscopic prisms.

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OPHTHALMIC PRISMS CORRECTIVE AND METRIC

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CORRECTIVE PRISMS

Seventy-five years ago, in 1870, lenses were still being prescribed in terms of their radii of curvature (a description) rather than in terms of their power (an operational specification). Twenty years later the metric operational system of numbering lenses according to the work they did (in refracting light rays) was almost universal, and this proved to be so much more satisfactory that progressive ophthalmologists began to turn their attention to similar problems with prisms, which were labeled in terms of the apex angle, a unit of shape rather than a unit of strength.

In 1887 Jackson¹ examined the prisms in seven trial cases, representing four well known manufacturers, he found that "in only one set did they all come within 16 per cent of the proper standard," and recommended that prisms should be marked according to their angle of minimal deviation. Landolt approved this recommendation, and a committee (Landolt, Burnett and Jackson) was appointed to present the proposition to the Tenth International Medical Congress, to be held in Berlin in 1890.

Before this meeting was held, however, Dennett² proposed to the American Ophthalmological Society a new unit, the centrad (∇), an operational unit specifying that in the position in which only one surface contributes to the deviation, the deviation shall be measured in hundredths of a radian. The centrad was thus a power measurement of the arc of the deviation produced. At the annual meeting of the American Ophthalmological Society in 1890, this unit, the centrad, was officially accepted³.

From the Knapp Memorial Laboratories, Institute of Ophthalmology

¹ Jackson, E. The Designation of Prisms by the Angular Deviation They Cause, Instead of by the Refracting Angle, *Tr Internat M Cong* (Sect 11) **3** 785, 1887

² Dennett, W S. A New Method of Numbering Prisms, *Tr Am Ophth Soc* **5** 422, 1888-1890

³ *Tr Am Ophth Soc* **5** 467, 1888-1890

In the meantime Charles Prentice, a New York optician, had devised yet another operational metric unit, the prism diopter (Δ), a description of which was published in the *Archives of Ophthalmology* in January 1890.⁴ The prism diopter is an operational unit, that is, it specifies work done, it is simple to understand and it fits into the metric system with a pleasing analogy to the dioptric system in specifying lens strengths. The prism diopter specifies that in the position in which only one surface contributes to the deviation, the deviation shall be measured on a tangent scale at a distance of 1 meter, each centimeter of deviation representing 1 prism diopter (1Δ). This unit has grown in usage and importance until at present it is practically universally employed (at least in America) for specifying and calculating the prismatic effects to be incorporated into ophthalmic corrective lenses.

At the Tenth International Medical Congress, held in Berlin in 1890, the Landolt, Burnett and Jackson report was discussed, but no action was taken.⁵

In the years 1889 to 1892 considerable acrimonious discussion took place, chiefly between the advocates of the prism diopter and those of the centrad. Owing to the lucid and satisfactory analyses of the problems encountered in calculating and incorporating prism effects in corrective lenses and to the development of an accurate prismometer and the use of prismatic scales, the prism diopter of Prentice gradually gained the ascendancy, which it has held to this day.

Since these discussions practically always revolved about the use of corrective, or therapeutic, prisms (as opposed to metric, or measuring, prisms of higher power), an important fact was usually overlooked. In order to attain the simplicity of either the centrad (∇) or the prism diopter (Δ) an unusual condition must be intro-

⁴ Prentice, C F. A Metric System of Numbering and Measuring Prisms, *Arch Ophth* **19** 64 and 128, 1890

⁵ *Tr Internat M Cong* **4** 49 1890

duced into the method of measurement. This condition, imposed both by Dennett and by Prentice, requires that *all refractive effect must take place at one surface*. Stated in this manner, the implication is rather startling, but this is the equivalent of specifying, as they both did, that the angle of incidence on the first surface must be zero, i.e., the prism is to be held with its first surface normal to the ray which is to be refracted. Thus all effect must take place at the second surface, and, as in the vertex specification of ophthalmic lenses, this gives a definite and easily located plane from which to make measurements.

Thus, four methods of numbering prisms are available:

1 The dimensions of the apex angle (α), expressed in degrees ($^{\circ}$)

2 The actual deviation, in degrees produced by the prism when it is set at its position of minimal deviation, i.e., when the ray within the prism is perpendicular to the line bisecting the apex angle ($\delta^{\circ} \text{ min}$)

3 The centrad (∇) or arc centume. This is an angular measurement of the deviation, equaling as the name indicates, one hundredth of a radian. On the arc of a circle of 1 meter radius each centimeter of deviation would equal 1 centrad. The incident ray must be normal to the first surface.

4 The prism diopter (Δ), or tangent centume. This expresses a linear, or tangential, measurement. With the incident ray perpendicular to the first surface, the prism diopter notation expresses the number of centimeters of displacement produced by the prism as measured on a tangent plane situated 1 meter from the second surface.

As has been seen the apex angle (α) does not tell what deviation will be produced unless one knows the refractive index and the position in which the prism is held.

The minimal deviation ($\delta^{\circ} \text{ min}$) is the most exact, scientific and satisfactory specification since it precisely expresses the angular deviation produced at an exact and symmetric position. It is the specification universally used by physicists. From the ophthalmologic viewpoint it has the disadvantage that the angle of incidence of entering light continuously varies with the apex angle and from this viewpoint some fixed position of holding is desirable.

The centrad has no particular advantage over the prism diopter. It expresses an exact deviation, but only when the position of holding is known.

For all practical uses, in specifying prisms to be incorporated with lens prescriptions (up to 8Δ) the departure from the specification that the incident ray is to be normal to the surface is unimportant, and the advantages accruing from simple and easy calculation leave the Prentice system far in advance of any other method of notation.

METRIC PRISMS

With metric prisms (prisms used for measuring high degrees of deviation, as in strabismometry) the situation is quite different, and the Prentice method offers many pitfalls and serious dangers. An extensive series of measurements and calculations of prisms to be used for this purpose is being undertaken and will be reported by one of us later. In justice to Prentice, it should be noted that the faults found with this system should not be attributed to him (he was concerned chiefly with corrective prisms, for which his system serves admirably). The dangers arise from the uncritical use of a system under conditions in which its faults are most glaringly manifest.

Our present purpose is to note the conditions on which the Prentice system is based and to report measurements begun thirteen years ago by one of us (L H H) and recently carried to completion by the group.

In 1890 prisms were not commonly used to measure strabismus. Most squints were estimated by the Hirschberg method, or the deviation was measured on the perimeter. The latter method is still the choice of most European and of many American ophthalmologists. Not until twenty years later, largely under the influence of Duane, was the prism and cover test popularized. This method is now widely taught and used, particularly in America.

As we have noted, in 1890 and for a long time thereafter, most prisms were numbered according to the degrees ($^{\circ}$) encompassed by their refracting angle (α). Many prisms still in use are so marked, and manufacturers are not uniform in their notations. No set of standards has been universally employed, and few if any manufacturers indicate in their markings the unit used. Some manufacturers continue to use the apex angle as a unit for marking, others label prisms in terms of minimal deviation in degrees, and still others use the prism diopter, almost all, however, failing to indicate the unit used.

As a result prisms bearing the same label vary widely in their powers of refraction, and the owner of a set is liable to be misled in interpreting the results of his measurements.

In 1931 one of us (L H H) conducted measurements on eleven sets of prisms belonging

to himself, his friends and various ophthalmic clinics. The results showed wide variations. Last year further elaborations for measurements were set up and the data extended to include twenty sets of prisms, two of which were sets of plastic prisms.

METHOD

Light from a 6 ampere ribbon filament (*A*, fig 1) was collimated, passed through a mask (*B*), a narrow vertical slit (*C*), a 73 Eastman Wratten monochromatic filter (*D*) to a condensing lens (*E*), positioned to collimate rays proceeding from the slit. The central beam was selected by a mask over the first surface of the condensing lens, and over the lower half of the second surface was placed a covering which carried an accurate line positioning the optical axis of the beam. At the other end of the optical bench was placed a transit head goniometer, which gave vernier readings to 1 minute. This was supplied with two accurately ground positioning plates, so that the location of the second face of the prism was exact and its distance from the receiving surface was precisely 1 meter. Elaborate measurements were taken to insure the correct prism to screen measurement, and the correct (90 degree) angle between the optical axes and the screen surface. The receiving sur-

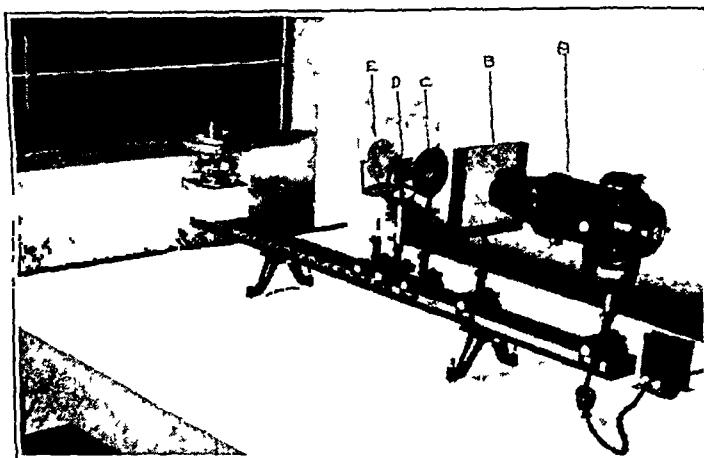


Fig 1.—Apparatus used in checking and measuring prisms

face was a frosted white glass. The measurement of tangent deviations were accurate to ± 0.5 mm.

All measurements were made as tangent values and checked against goniometric readings.

Measurements were made of the apex angle (α) of each prism, of its deviation in the position of minimal deviation, of its deviation in the Prentice position, and of its deviation in two other positions, to be discussed later (the "split positions" and the two positions of maximal deviation, when possible). Frequent checks were made by positioning the prism for a right or a left hand reading (reversing apex for base and first surface for second surface). The apex angle (α) was checked by reflecting the slit beam back along its course first from one surface and then from the other surface, and a final check on the accuracy of the measurements was made by calculating the index of refraction from the formula involving apex angle and deviation. A variation of more than 0.004 of the index required rechecking of all measurements of a given prism.

RESULTS

The results are shown in figure 2.

The column marked Δ gives the power of the prism as measured in the Prentice position, and

the column marked E gives the error expressed in prism diopters (Δ).

It is immediately apparent that the numbers on some sets of these prisms (sets 1, 2, 3, 4, 5, 12 and 20) refer to apex angles rather than to prism diopters. If this were not true, they would be in error over 100 per cent in some cases. For example, the prism marked 40 in set 1 actually has a power of 81Δ in the Prentice position, and this corresponds roughly with its apex angle ($40^\circ 10'$), while the prism marked 50 could not be measured in the Prentice position since its apex angle ($50^\circ 2'$) was greater than the critical angle of glass ($41^\circ 2'$)—when this prism was used in the Prentice position, total internal reflection took place. The same is true of sets 2, 3, 4, 5, 12 and 20.

Of the prisms apparently marked in prism diopters, the set of plastic prisms (no 6) was slightly strong in the lower powers (greatest error, 12 per cent for 8Δ) and slightly weak in the higher powers (about 10 per cent too weak for 40Δ , 45Δ and 50Δ). Errors among the glass prisms were not distributed regularly and bore no relation to strength except that, as might be expected, the higher powers tended to show greater total errors.

Reasonable manufacturing tolerances for ophthalmic measuring prisms would be as follows:

	Allowance
Up to 5Δ	0.06Δ
5Δ to 9Δ inclusive	0.12Δ
10Δ to 12Δ inclusive	0.25Δ
14Δ , 16Δ and 18Δ inclusive	0.37Δ
20Δ , 30Δ and 40Δ inclusive	0.50Δ

Most of the prisms we measured did not meet these tolerances, especially in the higher powers.

Most prism sets we examined did not have a manufacturer's label to indicate their source. None of them had an identifying unit to indicate the significance of the numeric label.

The importance of this lack is obvious and is well illustrated by the two sets of prisms 11 and 12. These two sets came from the office of a well trained and careful ophthalmologist. If they were properly used, a squint with a deviation of 40Δ would be exactly neutralized by the 40Δ prism in set 11, but if set 12 should be chosen, a squint with a deviation of 78Δ would be neutralized with the 40Δ prism.

These results show only the errors found when we were measuring prisms under rigid, specified conditions. Many other measurements were made in checking the apex angle (α), the minimal deviation produced by each prism ($\delta^\circ \text{ min}$)

and the two maximal deviations when possible (δ° max, $i=90^{\circ}$ and δ° max, $e=90^{\circ}$) as well as the deviation produced in a newly specified position ($\delta\Delta$ split). A tremendous effect can be produced on the deviation caused by a prism by departing from the conditions specified, i.e., by permitting the angle of incidence to deviate from zero. These measurements confirmed by calculated values will be reported by one of us later.

SUMMARY

The prism diopter (Δ) is a unit invented and introduced by Prentice, an optician to denote the operational power of ophthalmic prisms.

artificial condition namely, that the surface of incidence shall be normal to the path of the entering ray. While this condition has no practical significance for prisms of the powers used in corrective lenses, it has a high degree of significance for strong metric prisms used in measuring strabismus.

Some sets of prisms used by ophthalmologists are calibrated in prism diopters (Δ), others are calibrated in terms of the apex angle, in degrees ($^{\circ}$). The unit of calibration is rarely given. This results in possible errors due to misconception of the unit used, of over 100 per cent in the higher powers. In the lower powers such errors are insignificant for practical clinical

SET	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20																												
Δ	Δ	E	Δ	E	Δ	E	Δ	E	Δ	E	Δ	E	Δ	E	Δ	E	Δ	E	Δ																													
5	4	-1	5			6	+1		6	+1	4	-1	5	4	-1	6	+1	4	-1																													
1	10	10	10	11	+1	9	-1	10	9	-1	10	11	+1	9	-1	10	10	11	+1	10																												
2	17	-3	19	-1	20	21	+1	20	20	20	21	+1	20	19	-1	20	19	-1	20	20																												
3	29	-1	30	30	30	29	-1		30	28	-2	30		30	30	29	-1	30	28	-2	30																											
4	40	40	39	-1	40	39	-1	41	+1	40	41	+1	41	+1	40	40	35	-5	40	39	-1																											
5	50	51	+1	50	51	+1	50		50	49	-1	50	49	-1	44	-6	48	-2	50	47	-3	50																										
6	60	58	-2	58	-2	56	-4	58	-2	61	+1	60	60	59	-1	58	-2	60	60	59	-1	58	-2	51	-9																							
7	70	69	-1	70	69	-1	70		68	-2	69	-1	70	70	69	-1	61	-9	68	-2	68	-2	69	-1	70																							
8	78	-2	78	-2	80	79	-1	84	+4	90	+0	80	78	-2	79	-1	77	-3	79	-1	73	-7	78	-2	78	-2	79	-1	70																			
9	80	10	90	89	-1	91	+1	90		90	89	-1	89	-1	89	-1	90	82	-8	90	88	-2	89	-1	89	-1	91	+1	88	-2	91	+1	81	-9														
10	10.0	9.8	-2	10.1	+1	9.8	-2	9.8	-2	10.2	+2	9.8	-2	9.7	-3	10.0	9.9	-1	10.0	9.8	-2	9.5	-5	9.8	-2	9.7	-3	10.0		9.8	-2	9.8	-2	10.4	+4													
11	11.0	11.0				11.8	+8				10.9	-1	10.7	-3	10.6	-4	10.9	-1						10.7	-3	10.6	-4	10.8	-2			10.8	-2															
12	12.0	11.8	-2	11.8	-2	10.8	-2	12.5	+5	11.8	-2	11.8	-2	11.7	-3	11.8	-2	12.0	11.9	-1	11.7	-3	11.7	-3	11.9	-1	11.7	-3	11.7	-3	11.7	-3	11.1	+1														
13	13.1	+1	12.9	-1		13.1	+1				12.8	-2	12.8	-2	12.8	-2								12.8	-2																							
14	13.0	13.9	-1	12.9	13.1	12.8	-12	13.8	-2		13.8	-2	13.8	-2	13.6	-4	13.7	-3	14.0	13.0	-10		13.7	-3	13.8	-2	13.7	-3	14.0		13.6	-4	14.0		13.0	10												
15	14.9	-1	15.0			14.9	-1				15.2	+2	14.7	-3	14.8	-2	14.8	-2						14.7	-3			14.8	-2	14.8	-2	14.7	-3			14.7	-3											
16	15.8	-2	16.0			15.8	-2	16.2	+2	14.5	-5			15.7	-3	15.7	-3	15.8	-2	15.6	-4	15.9	-1	15.4	-6			15.6	-4	15.7	-3	15.8	-2	15.5	-5	15.6	-4	15.7	-1									
18	18.2	+2	17.6	-4	17.4	-6	17.9	-1	18.0					18.0	17.4	-6	17.3	-7	17.4	-6	18.0	17.8	-2		17.6	-4	17.4	-6	17.4	-6			17.6	-4			17.9	-1										
20	19.9	-1	19.8	-2	20.1	+1	19.8	-2	20.0		20.2	+2	19.5	-5	19.7	-3	19.2	-8	19.4	-6	20.0	20.1	+1	19.7	-3	19.2	-4	19.7	-3	19.3	-7	19.5	-5	17.9	-2	19.6	-4	20.2	+2									
25	26.9	+19	27.1	+21		27.5	+25	27.4	+29	25.7	+7	27.3	+23	24.2	-8	24.3	-7	24.3	-7					24.7	-3			24.2	-8	24.3	-7	24.6	-4			24.6	-4											
30	36.6	+6.6	30.3	+3	37.1	+7.1	36.7	+6.7	36.5	+6.5	27.3	-2.7	36.4	+6.4	29.1	-9	29.3	-7	29.1	-9	30.2	+2	36.8	+6.8	29.1	-9	29.4	-6	29.1	-9	29.9	-1	29.5	-5	29.5	-5	38.5	+8.5										
35											33.1	-19			33.5	15	33.1	19						31.8	32			33.6	-14	33.1	-19	34.7	-3			34.7	-3											
40	81.0	+4.0	80.2	+4.0	76.3	+36.3	76.9	+26.9	74.3	+34.3	35.3	-37	39.9	-1	37.8	-22	37.0	30	37.3	-27	40.0	78.3	38.3	36.0	40	38.2	1.8	37.8	-22	37.0	-30	38.6	-14	38.1	-19	38.5	-15	90.7	50.7									
45															40.8	-42																																
50																45.8	-42	43.4	-6.6	46.2	-3.8	46.7	33	48.1	19																							

Fig 2.—Results of measurements on twenty sets of prisms. The first column at the left indicates the number borne by the prism—presumably prism diopters (Δ). Under each set number the left hand column, marked Δ , indicates the measured power of the prism, and the right hand column, marked E , indicates the error, expressed as + (too strong) or - (too weak).

It was intended to be used mainly for corrective prisms, and in this respect the concept has great value, particularly in facilitating the work of the optician who is required to incorporate prismatic effects into a prescription for lenses. By extension, the unit was utilized to express the strength of all prisms up to a theoretic limit of 115Δ (or up to that prism whose apex angle coincides with the critical angle of the medium used).

To achieve this simplification, Prentice was forced to incorporate into his system a highly

purposes. The purchaser of a set of prisms is entitled to know the unit used, and this should be clearly marked on each prism.

Measurements made on twenty assorted sets of prisms indicated that many of them have errors exceeding reasonable manufacturing standards.

In use of prisms labeled with the Prentice system great care must be observed to comply with the conditions on which this system is based, otherwise high errors will be introduced by inaccurate positioning.

OCULAR SEQUELAE OF ADMINISTRATION OF GENERAL ANESTHESIA

PARALYSIS OF THE SUPERIOR RECTUS MUSCLE EXOPHTHALMOS, PSEUDOPTOSIS AND
FIBROSIS OF THE INFERIOR RECTUS MUSCLE FOLLOWING AN OPERATION FOR
PILONIDAL CYST WITH THE PATIENT UNDER GENERAL ANESTHESIA

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A search of the literature revealed only one report of paralysis of the extraocular muscles associated with general anesthesia¹ other than spinal anesthesia. In Woltman's report 2 cases are described. However, there have been approximately 175 cases of paresis of the extraocular muscles related to the use of spinal anesthesia² and 1 case in which this condition was associated with local anesthesia administered for tonsillectomy³.

In the case to be described, paralysis of the right superior rectus muscle, pseudoptosis of the right upper eyelid, exophthalmos of the right eyeball and fibrosis of the right inferior rectus muscle were diagnosed after administration of ethylene-ether anesthesia for an operation for pilonidal cyst.

REPORT OF A CASE

F W, a patrolman aged 36, was operated on for pilonidal cyst on Jan 29, 1942, under ethylene-ether anesthesia. Prior to this operation the patient's eyes revealed no abnormality.

Within twenty-four hours after the operation the patient experienced diplopia when looking upward. On

From the Research Department of the New York Eye and Ear Infirmary

This study was aided by a grant from The Ophthalmological Foundation, Inc.

Presented before the Section of Ophthalmology of the New York Academy of Medicine, May 15, 1944

1 Woltman, H W Post-Operative Neurological Complications, Wisconsin M J **35** 427, 1936

2 Levine, J Paralysis of Extra-Ocular Muscle After Spinal Anesthesia, Arch Ophth **4** 516 (Oct) 1930 Fawcett, K R Extra-Ocular Muscle Paralysis Following Spinal Anesthesia, Minnesota Med **14** 648, 1931 Biggam, J Paralysis of Ocular Muscles Following Spinal Anesthesia (with Stovaine), Brit J Ophth **16** 552, 1932 Blatt, N Ocular Paralysis After Spinal Anesthesia, Wien klin Wchnschr **41** 1048, 1928

3 Kiraly, J Paralysis After Anesthesia of Tonsils for Tonsillectomy, Arch f Ohren-, Nasen- u Kehlkopf **138** 119, 1934

the following day diplopia was present while he was reading. The onset of ptosis was coincidental with the diplopia.

On Feb 18, 1942, three weeks after the operation for pilonidal cyst, examination of the eyes revealed that vision without correction was 20/20 in each eye, the near point of accommodation for the right eye was 180 mm for 400 mm print, and the near point for the left eye, 180 mm for 300 mm print. The reading of the exophthalmometer, set at 97 mm, was 19 mm for the right eye and 14 mm for the left eye. Protrusion of the right eye was straight forward and completely reducible on pressure, and there was no retrobulbar tenderness or tumor of the eyeball. The right cornea was hypersensitive to touch. The levator muscle was not paralyzed, but the depression of the eyeball made elevation of the upper eyelid difficult. The pupils were equal in size and reacted promptly to light and in accommodation. The media and the fundi were normal. The right eye could be elevated to within 5 degrees of the primary position with slight extorsion. There was no action of the right superior rectus muscle. Abduction was excellent, but adduction was slightly limited. The eyelids opened and closed normally. The patient wrinkled his forehead normally. Sensitivity of the skin and of the conjunctiva was normal.

Physical examination revealed no abnormalities. The blood pressure was 140 systolic and 86 diastolic. The pulse rate was 80. Neurologic examination gave negative results except for the findings referable to the eye. No bruit was heard.

All the laboratory tests made within six weeks after the operation gave normal results. Lumbar puncture, a colloidal gold test and a Wassermann test revealed nothing significant. An electroencephalogram was normal. The urine was normal except for an occasional leukocyte. The basal metabolic rate was +6, +12 and +1, respectively, on three occasions. The blood cholesterol content was 240 mg per hundred cubic centimeters. The blood iodine level was normal (8 micrograms per hundred cubic centimeters). Two roentgenograms of the skull, including the orbits, taken in February and November 1942, revealed no abnormality or pathologic change. The optic foraminae were normal in size and shape. A roentgenogram of the right orbit taken after injection of air into the peri-orbital tissues showed the eyeball to be normal in size and position, with no evidence of tumor. The visual fields were within normal limits.

On May 4, 1942 the right eye could be elevated upward only to 5 degrees below the primary position with slight extorsion.

Examination one year later revealed that there was essentially no change in the condition of the eyes. Examination of the eyes preoperatively on Dec 7, 1943, eleven months after the onset, revealed the following status. The upward limit of fixation of the right eye had remained at 5 degrees below the horizontal plane. The eyeball, even with forceps, could be rotated upward only to the horizontal plane. The muscle balance, determined with the cover and parallax test, was 15 prism diopters of exotropia and 78 prism diopters of left hypertropia at 6 meters, and 22 prism diopters of exotropia and 78 prism diopters of left hypertropia at 25 cm. The findings in the diagnostic positions of gaze at 75 cm, with the cover test and prisms, were charted as follows:

	Right	Left	
Eyes Right and up	LHT 90Δ plus and up	LHT 90Δ Eyes Left XT variable	
Right	LHT 80Δ	LHT 78Δ Left XT 12Δ	
Right and LHT 78Δ down	LHT 64Δ XT 12Δ	Left and down	

In this tabulation LHT and XT indicate left hypertropia and exotropia respectively.

Study of the motor anomaly revealed complete loss of elevation in the field of activity of the right superior rectus muscle and severe secondary deviation of the left inferior oblique muscle. The elevating power of the right inferior oblique muscle could not be determined accurately, although the slight elevating power that was

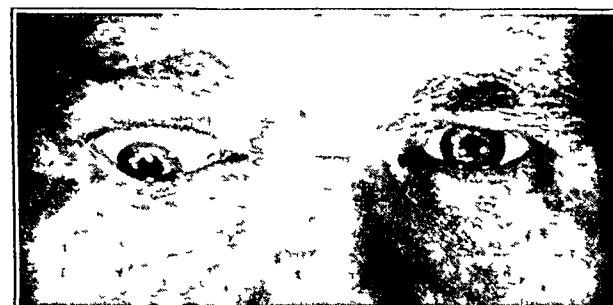


Fig 1.—Preoperative appearance of the eyes in the primary position, showing severe right hypotropia, exophthalmos and right pseudoptosis.

present seemed to be produced by that muscle. The right inferior rectus muscle showed considerable contracture. There was also severe secondary deviation of the left superior oblique muscle.

The preoperative diagnosis was paralysis of the superior rectus muscle, exophthalmos, right pseudoptosis, partial paralysis of the inferior oblique muscle and fibrosis of the inferior rectus muscle of the right eye.

On Feb 9, 1943, the following surgical procedure was performed: complete tenotomy of the right inferior rectus muscle at the insertion, resection of 8 mm of the right superior rectus muscle and transplantation of the inferior half of the right lateral rectus muscle to the temporal half of the stump of the inferior rectus muscle (fig 2). The upper half of the lateral rec-

tus muscle was reattached to the lower half of the insertion of the lateral rectus muscle. There were no adhesions about the inferior rectus muscle, but there was absolutely no elasticity of this muscle when upward traction was produced with a tenotomy hook. It seemed to be completely fibrosed.

On March 1, 1943, three weeks following the operation, with the cover and parallax test the patient had orthophoria for distance (6 meters) and exophoria of 10 prism diopters for near (25 cm) vision (fig 3). The findings in the diagnostic positions of gaze with the cover test and prisms at 75 cm were charted as follows:

	Right	Left
Eyes Right and up	XT 12Δ LH 10Δ	XT 20Δ LH 9Δ
Right	XT 8Δ RH 3Δ	XT 20Δ LH 5Δ
Right and down	XT 8Δ RH 16Δ	Left and down LH 3Δ

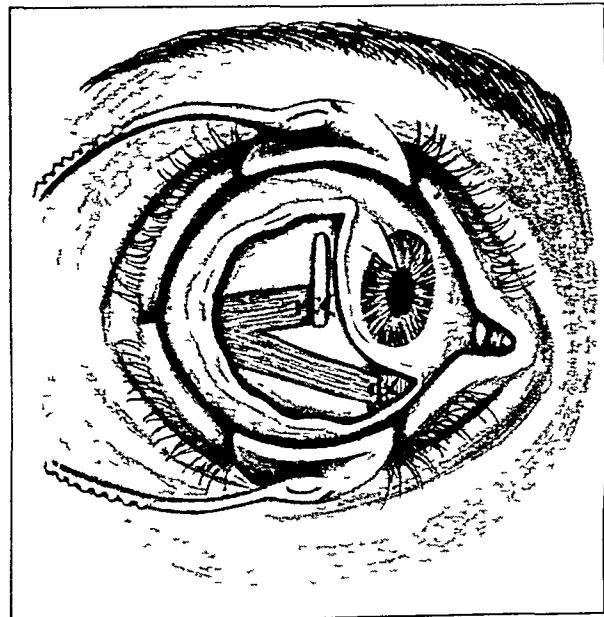


Fig 2.—Illustration showing transplantation of the inferior half of the right lateral rectus muscle to the temporal half of the stump of the inferior rectus muscle and reattachment of the upper half of the lateral rectus muscle to the lower half of the lateral rectus insertion.



Fig 3.—Postoperative appearance of the eyes in the primary position. With the cover and parallax test the patient had orthophoria for distance (6 meters) and exophoria of 10 prism diopters for near vision (25 cm).

Three weeks after the operation, the patient obtained fusion, according to the Worth four dot test, at 6 meters and at 25 cm. The patient's near point of convergence was 80 mm. Slight weakness of the right superior rectus muscle and secondary overaction of the left inferior oblique muscle persisted. Underaction on depression in the field of activity of the right inferior rectus muscle continued. However, considerable improvement in ability to depress the right eye was noticed after several weeks. The right inferior oblique muscle recovered almost all of its normal power of elevation. The patient complained of diplopia when he looked upward, upward and inward, and upward and outward; he obtained fusion in other parts of the field (fig 4). The lower eyelid was still displaced somewhat downward.

In January 1944, eleven months after the operation on the ocular muscles, the exophthalmos of the right eye seemed to have increased. This was verified by three different exophthalmometric readings taken during January and February 1944. The average of the three readings, with the exophthalmometer set at 98 mm, was 22 mm for the right eye and 16 mm for the left eye. The exophthalmometric reading taken in February 1942, one year prior to the operation on the eye, with the instrument set at 97 mm, was 19 mm for the right eye and 14 mm for the left eye. Since the patient has no ocular symptoms, the eye is not tender and the proptosis is reducible, we believe that the increase in the exophthalmos may be the result of the tenotomy of the fibrosed inferior rectus muscle.

COMMENT AND CONCLUSIONS

The most probable explanation of the mechanism by which the operation for pilonidal cyst with the patient under general anesthesia caused paralysis of the right superior rectus muscle, exophthalmos and complete fibrosis of the inferior rectus muscle was that an embolism of the artery supplying the superior rectus muscle occurred. Fibrosis of the inferior rectus muscle may have been caused by the secondary contracture associated with embolic myositis.

A specimen of the inferior rectus muscle was not obtained for biopsy because of extensive depression and fibrosis.

It was thought before operation that numerous adhesions existed between the muscle and the eyeball as a result of inflammation but none was found.

There may be no proved causal relation between the operation with the patient under ethylene-ether anesthesia and the sudden onset of diplopia and the proptosis, but the short interval of less than twenty-four hours between the occurrence of the ocular symptoms and the operation is highly suggestive of a close relationship. It seems reasonable to believe that the

condition of the eye could have been present some hours before it was noticed.

The severe vertical strabismus was remedied by complete tenotomy of the inferior rectus muscle, resection of 8 mm of the superior rectus muscle, transplantation of the lower half of the lateral rectus muscle to the temporal half of the stump of the inferior rectus muscle and reattachment of the upper half of the lateral rectus muscle to the lower half of its stump. It was difficult to decide what procedure was indicated in this case, but the resulting useful field of binocular fixation indicates that the technic employed was reasonably sound physiologically.

35 East Seventieth Street

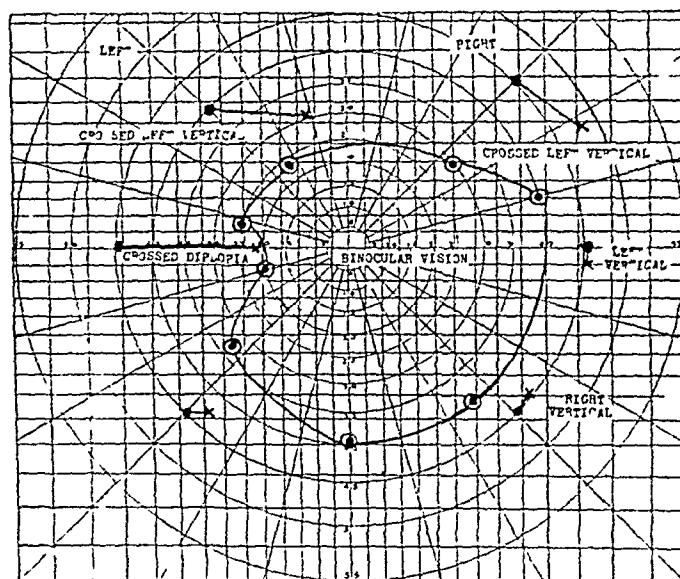


Fig 4.—Field of diplopia and field of binocular fixation on March 1, 1943, three weeks following the operation. The amount and nature of the diplopia, plotted at 75 cm, was determined with a red glass over the left eye and the right eye fixing.

DISCUSSION

DR CHARLES ALLEN PERERA, New York. Do the authors think there is any similarity between this case and the cases of orbital myositis reported before this section last year by Dr Dunnington and Dr Berke (Exophthalmos Due to Chronic Orbital Myositis, *ARCH OPHTH* 30: 446 [Oct] 1943)? The onset is different, but the clinical picture is the same and the observations at operation are similar. The suggestion of an inflammatory embolic cause in the case reported may give a clue to the cause of the orbital myositis.

DR RUDOLF AEBELI, New York. What explanation is offered for the exophthalmos which is present and why could the eye not be raised above the horizontal plane if there were no adhesions below at the time of the operation?

DR RALPH I LLOYD, Brooklyn What anesthetic was used?

DR ISADORE GIVNER, New York How long after the appearance of the symptoms was surgical intervention carried out?

DR GIOVANNI PACCIONE, New York Was diabetes ruled out?

CAPTAIN GERALD FONDA, M C , A U S To answer the last question first Both the amount of sugar in the blood and the results of urine analysis proved that diabetes was not present

Dr Lloyd, anesthesia was induced with ether and ethylene

Dr Aebli, the eye cannot be elevated, even with fixation forceps, because of the extensive fibrosis of the muscle

Dr Perera, I believe that in chronic orbital myositis there is a progressive inflammatory process with fusiform enlargement of muscle, and there are at times adhesions between the orbit and the muscle In this case no adhesions were discovered between the muscle and the orbit, and no fusiform enlargement of muscle was found The myositis was acute and was localized in the inferior rectus muscle, resulting in fibrosis

Dr Givner, the operation on the eye was done thirteen months after the onset of ocular symptoms

GLAUCOMA ASSOCIATED WITH NEVUS FLAMMEUS

REPORT OF A CASE

MAJOR ERWIN E GROSSMANN
MEDICAL CORPS, ARMY OF THE UNITED STATES

The occurrence of glaucoma with nevus flammeus is uncommon, although not rare, in both the foreign and the American literature. The condition was first described by Schirmer in 1860, in association with buphthalmos, and since then several others have added to the picture to warrant its acceptance as a clinical entity manifested by nevus flammeus, glaucoma, epileptiform seizures, nevi and dilated vessels in the conjunctiva, iris and choroid.

Of the many observations made in cases of this syndrome few have agreed concerning the mechanism of the glaucoma, indeed, etiologic theories have varied sufficiently to permit O'Brien and Porter¹ to state that the cause was unknown. From the evidence in many of the reported cases and in the present case it appeared that perhaps another mechanism not associated with increased intraocular pressure may be the cause of the glaucomatous atrophy of the optic nerve.

REPORT OF CASE

The patient, aged 29, born in Wisconsin, was seen in the outpatient clinic on March 2, 1943. He presented no complaints but had come in for examination during a routine survey of all ocular defects at the Army Post. He gave the following history. He had had poor vision in the left eye since the age of 12 years, but medical attention was never requested. Since the age of 18 or 19 all vision, even perception of light, had been gone in this eye. He had had "fainting spells" since the age of 17 and had had three such attacks during the past six months. He was hospitalized twice, and a tentative diagnosis of epilepsy was made on his second admission to the hospital. He stated that he had never had any discomfort or pain in the left eye. The family history was noncontributory.

Examination revealed that the patient was physically sound, with a port wine nevus involving the left side of the face, including the forehead, temple and cheek. Both the upper and the lower eyelid were partially involved, as well as the lower palpebral conjunctiva and two thirds of the bulbar conjunctiva. One large tortuous conjunctival vessel coursed about the entire circum-

ference of the cornea, about 15 mm from it, giving off small branches to the limbal area. The cornea measured 12 mm in the horizontal diameter, and the anterior chamber appeared to be of normal depth. The pupil was semidilated and reacted sluggishly to light. Slit lamp examination did not reveal any new vessels in the iris or any aberrations except for a remnant of persistent pupillary membrane, which extended from 9 to 12 o'clock. The lens and the vitreous were clear, and the fundus revealed a pronounced degree of glaucomatous cupping, the vessels bending at a right angle as they dipped over the scleral rim and soon being lost in a whitish, fluffy mass of what appeared to be scleral supporting tissue. There was no evidence of choroidal atrophy or signs of angioma. The vessels appeared to be normal in caliber and were less tortuous than normal. The tension was determined on two separate days and at different times of the day. Four readings showed 19, 21, 20 and 23 mm (Schiøtz). Vision was nil, with no perception of light. The right eye was normal in all respects, and determinations of the tension made at the same time as those on the left eye showed 11, 14, 12 and 12 mm (Schiøtz). The field of vision, both central and peripheral, was normal. Neurologic studies showed nothing abnormal and dermatologic examination revealed, in addition to the nevus described previously, a pea-sized hemangioma on the face near the hair line of the left temple.

Roentgenograms of the skull did not reveal any calcification of the meningeal vessels. Laboratory tests gave normal results. Both eyes were dilated with 2 per cent solution of homatropine hydrobromide, which was instilled three times at five minute intervals, the tension was determined before each instillation and, again, thirty minutes and one hour after the first instillation. No increase in tension was noted in either eye. The patient was given 1,000 cc of water, and the tension was determined before and one hour after the water was drunk. No elevation of tension was noted in either eye, the difference between the first and the last reading varying only 1 mm of mercury (Schiøtz). Gonioscopic facilities were not available.

COMMENT

No attempt has been made to review the literature, inasmuch as O'Brien and Porter¹ thoroughly covered the field in 1933 and Ehrlich² recently cited freely many of the other observers. The etiology was discussed fully by O'Brien and

From the Department of Ophthalmology, Regional Hospital, Camp Mervin, Texas.

¹ O'Brien, C S, and Porter, W C. Glaucoma and Nevus Flammeus, Arch Ophth 9: 715 (May) 1933.

² Ehrlich, L H. Bilateral Glaucoma Associated with Unilateral Naevus Flammeus, Arch Ophth 25: 1002 (June) 1941.

Porter Ehrlich expressed the opinion that the occurrence of epileptiform seizures is exceptional, but the association is frequent enough to warrant one's anticipating this symptom in every case Mehney³ stated that usually nevus flammeus is not associated with glaucoma unless the nevus involves the lids or other ocular structures, and he speculated whether nevus involving these structures occurs without glaucoma.

In the case reported here, although deep glaucomatous cupping was present, no evidence of increased intraocular pressure was noted Bar⁴ described a similar case in which both eyes were involved, one showed partial excavation of the disk and the other merely a pale disk, but no glaucoma Lowenstein⁵ reported a case in which nevus flammeus occurred in a woman aged 40 who also had partial excavation of the disk but no elevation in tension, her visual fields and vision were normal McRae⁶ reported a case in which there was a goblet-shaped cavity in the optic nerve head but no increase in tension He stated the belief that the condition was pseudoglucoma O'Brien and Porter reported a case of deep glaucomatous cupping with a tension of only 12 mm (Schiotz) and concluded that it was an instance of arrested hydrophthalmos.

Therefore the number of cases on record in which there was no evidence of glaucoma (increased intraocular pressure or instability of the pressure-regulating mechanism) but in which there was glaucomatous-like excavation of the disk is sufficient to warrant the assumption that the cupping is not always due to glaucoma but is simply, as McRae stated, pseudoglucomatous It does not seem logical to assume that glaucoma based on a congenital permanent defect, whether in the choroid or in the angle of the chamber, would in due time become arrested and finally manifest comparatively low tensions The provocative tests performed in this case caused no embarrassment of the mechanism for the exchange of intraocular fluid Yet the cupping of the disk in the left eye was of such a degree as is often seen only in the latest stages of glaucoma

³ Mehney, G H Nevus Flammeus Associated with Glaucoma, *Arch Ophth* **17** 1018 (June) 1937

⁴ Bar, C Ein bemerkenswerter Fall von Feuermaul und Glaukom, *Ztschr f Augenh* **57** 628, 1925

⁵ Lowenstein, A, abstracted, *Klin Monatsbl f Augenh* **70** 540, 1923

⁶ McRae, A Pseudoglucoma, *Brit J Ophth* **13** 63, 1929

Of possible significance was the large amount of scleral supporting tissue seen within the abnormal cup This suggests an anomaly within or about the optic nerve head, close to the cribriform fascia, which was weakened to such an extent that an intraocular tension as low as 19 to 23 mm of mercury (Schiotz) was sufficiently powerful to force it backward, dragging the nerve fibers along as they crossed the sharp rim of the scleral canal The tension in the right eye was constantly from 7 to 13 mm of mercury lower than that in the left eye, and this difference, together with the defect of the cribriform fascia, may have been sufficient to give rise finally to the typical glaucomatous cupping.

I do not offer the view that telangiectatic changes occurred behind the nerve head, for no abnormalities were grossly apparent, and the retinal and choroidal vascular systems seemed normal It is more likely that the defect was congenital, several congenital anomalies frequently occur together, without necessarily being related embryologically—for instance, the persistent pupillary membrane in the left eye in the case reported in this paper was an associated congenital defect It is entirely possible, therefore, that this syndrome is not always associated with glaucoma but that the latter is determined largely by the location of the congenital defect I suspect that if gonioscopic studies had been made in all cases reported a defect would have been found in the angles of the chamber in the cases with associated buphthalmos and that such a defect would undoubtedly be related to a nevoid condition, directly or indirectly In the cases in which the picture of adult glaucoma is presented, I should suspect the angles of the chamber to be open and functioning and the mechanism for the production of the glaucoma to be that for which Ehrlich expressed preference, namely that telangiectatic changes in the uvea, especially the choroid, result in disturbances in the exchange of intraorbital fluid In those cases reported previously, including the present one, in which no increase in the intraocular pressure was observed, the condition may well be pseudoglucoma This assumption is strengthened by the negative results of the provocative tests performed in the present case.

CONCLUSIONS

The occurrence of a case of nevus flammeus with ocular changes resembling the late stages of glaucoma affords an opportunity for further speculation as to the mechanism of the glaucoma.

In all cases of this syndrome the type of glaucoma is not necessarily the same, but depends on the region which may be affected by a con-

genital anomaly, thus, buphthalmos results if the angle of the chamber is completely closed, and the adult type of glaucoma, if the angle is incompletely involved, together perhaps with other anomalies of the uvea.

A third mechanism may be that suggested in this case, in which no true glaucoma could be proved to exist, i.e., there was no typical increase in the intraocular pressure, but glaucomatous cupping resulted from a congenitally

weakened lamina cribrosa, on which the exertion of a tension of 19 or 23 mm of mercury produced as pathologic an effect as would a tension of 40 or 50 mm of mercury in a normal eye.

Inasmuch as postmortem studies are infrequent in cases of this syndrome, gonioscopic examination would be invaluable in clarifying some of the conjectures concerning the mechanism involved in the production of glaucoma.

PATHOGENESIS OF GLAUCOMA

LEO HESS, M.D.
BOSTON

In two articles¹ a modest attempt has been made to give a more precise idea of the pathogenesis of the rise of intraocular pressure in acute glaucoma. This condition according to my concept, does not arise primarily in the eyeball but has its origin in certain nerve structures outside the eye—the ciliary ganglion, the important diencephalic vegetative center (Karplus-Kreidl center²), at the base of the brain, in the vicinity of the optic chiasm and in the cortex of the brain. Mistakenly, the signs of acute and of certain kinds of chronic glaucoma were once considered to be inflammatory. Actually, the classic signs of common inflammation—arterial hyperemia, exudation and migration of white cells—cannot be demonstrated either by clinical or, to any significant degree, by histologic studies. The same holds true of the so-called inflammatory signs following thrombosis of the vena centralis retinae. If any inflammation exists in either instance, it is of a peculiar type ("angioneurotic inflammation"?). The sudden onset of the glaucomatous attack reminds one of an acute crisis of the vegetative nervous system, e.g., the epileptic fit or the rapid development of edema of the lungs in association with diseases of the brain or the spinal cord (Hess³). The actual site of the crisis in acute glaucoma is the ciliary ganglion and the nerves and capillaries of the ciliary body. It develops there under the indirect influence of the cortex (*glaucoma emotivo*, of the Italian school) or under the immediate influence of the diencephalic center, whence the irritation is conveyed to the bulbus by way of certain nerves, to be discussed later. The crisis consists primarily of a vasomotor and secondarily of a secretory disturbance (in passing it may be mentioned that in the epileptic fit, as well as in acute edema of the lungs, it is the vasomotor nerves that play an eminent role). The bulbus is the terminal organ. The crisis is a constrictor, or pressor, one. This can be deduced (1) from the

narrowing of the terminal branches of the retinal artery after an attack⁴, (2) from the effect of miotics (Kadlicky, Thiel, Koller), resulting in vasodilation, (3) from the sudden rise of the systemic arterial pressure, which often antedates the attack, (4) from the arterial pulsation in the papilla after the attack and (5) from the experimental evidence, provided by Ebbecke, that the impairment of eyesight during increased intraocular pressure is dependent on ischemia of the retina. The importance of the changes in the other tissues (cornea, lens, corpus vitreum, optic nerve) should, however, by no means be underestimated.

The mydriasis being unquestionably sympathogenic,⁵ all the other signs of the acute attack as has been pointed out in the second article,¹ can be accounted for on a neurogenic basis. The headache, associated with nausea and vomiting, comparable to the headache and vomiting in cases of tumor cerebri and of migraine, the lacrimation, and the photophobia. The edema of the cornea (together with anesthesia, due to the edema) and the edema of the conjunctiva, lids and iris are likewise a nervous effect and are similar to angioneurotic edema (Quincke's edema fugax urticaria). The moderate rise of temperature, not infrequently met with in cases of acute glaucoma, can be traced to irritation of the heat center at the base of the brain, not far from the Karplus-Kreidl center (Ranson⁶). In addition to these symptoms, some indirect clinical signs and many pharmacologic observations could be referred to which are confirmatory, I believe, of the existence of a nervous factor underlying acute glaucoma. As an organ of sight, the eye-

4 The connection between acute elevation of the systemic blood pressure and heightened intraocular pressure is evidenced by the clinical experience that immediately after delivery both pressures are high. After intravenous injection of epinephrine into the ear vein of the rabbit, both the intraocular pressure and the blood pressure are elevated. With hypertension of chronic renal disease the intraocular pressure is not high.

5 Mydriasis is not secondary to a primary rise of intraocular pressure (Heine, L. Klin Monatsbl f Augenhe 40 25, 1902).

6 Ranson, S. W., in Harvey Lectures, Baltimore, Williams & Wilkins Company, 1936.

1 Hess, L. Pathology of Acute Glaucoma, Arch Ophth 26 250 (Aug) 1941, Pathogenesis of Acute Glaucoma, ibid 32 128 (Aug) 1944

2 Karplus, T. P., and Kreidl, A. Arch f d ges Physiol 129 138, 1909, 135 401, 1910 143 119, 1911, 171 192, 1918

3 Hess, L. Wien med Wochenschr 84 285, 1934

ball, the optic nerve and the primary and secondary optic centers within the brain represent one system. According to my concept, the eyeball, certain peripheral nerves, the ciliary ganglion and the diencephalic center also represent a unit concerned with the vital function of regulation of intraocular pressure.⁷ This functional unit is finally governed, as are all the functions of all the visceral organs, by the cortex. The purpose of this paper is to elucidate this point of view and to show how it applies not only to acute glaucoma but to all other forms of increased intraocular pressure, acute or chronic, primary or secondary. It is an attempt at a general theory of the cause of rise in intraocular pressure, an attempt which has not been made in the literature. This theory of the neurogenic origin of intraocular pressure may better enable one to differentiate the types of glaucoma and to evaluate the means of treatment at one's disposal. High intraocular pressure, however, is not identical with glaucoma. The same can be stated of the high arterial pressure which is the outstanding clinical sign of "essential hypertension." The essence and origin of the latter are as unknown as are the nature and cause of glaucoma.

Obviously, one is confronted with a certain nervous mechanism regulating the production inflow and outflow of the fluids of the eye. It may be compared to the mechanism which is thought to regulate the arterial pressure—a concept which has proved in recent years to be helpful in elucidating, differentiating and treating the various types of arterial hypertension.

In the production of the fluids of the eye two factors are to be borne in mind. 1. Mere transudation, largely dependent on the intracapillary pressure in the ciliary processes, an increase in which, according to Krogh, is associated increased permeability and increased escape of plasma. This hydrostatic pressure is opposed by the osmotic pressure of the protein bodies of the blood plasma.⁸ 2. An apparently true epithelial secretion of the ciliary body, which is known to be influenced by physostigmine and atropine in the same sense as are true glands (Seidel). The latter fact would lead one to suppose that there exists an influence of the vegeta-

⁷ Normally the intraocular pressure is maintained at an almost constant level, with small oscillations corresponding to the rhythm of the heart beat and the respiration. This can best be explained by neuroregulation and not by hormonal influences.

⁸ Artificial increase in the osmotic pressure of the blood plasma is always followed by lowered intraocular pressure (Duke-Elder, W S Brit J Ophth 10 513, 1926 Dieter, W Arch f Augenh 96 179, 1925)

tive nervous system on the ciliary body. The transudation, as far as it is dependent on the intracapillary pressure, is likewise regulated by nerve impulses. The outflow of the fluids of the eye, mainly through the spaces of Fontana and the canal of Schlemm into the anterior ciliary veins, takes place finally in the superior ophthalmic vein which is practically continuous with the cavernous sinus. Neither the superior nor the inferior ophthalmic vein is provided with valves, and it is generally impossible to state the direction of the blood flow within these veins. On the other hand, the sinus cavernosus is known to contain in its lateral wall the ophthalmic and the maxillary branches of the trigeminus. Hence it is likely that the blood stream within the ophthalmic and ciliary veins, and indirectly the inflow of the intraocular fluids, is connected with nerve impulses.⁹ There is no evidence of a primary blockade to the outflow of blood in the onset of acute glaucoma. The primary disturbance is suggested in the increased production and inflow of fluids. The amount of blood within the bulbus is connected with the venous return to the right auricle. Any venous congestion—due to strain on the heart muscle, compression of the jugular vein, or even administration of miotics, with sudden hyperemia within the eye—may result in an attack of glaucoma. Finally, it should not be forgotten that the wall of the eyeball, through its elasticity, may exert a certain influence on the pressure in the eye.

FIRST (CILIARY) REFLEX ARC

Physiologic Aspect.—The regulatory nervous mechanism I have in mind is necessarily a reflex mechanism, consisting, as does any reflex, of three portions, an afferent (proprioceptive) limb, an efferent (motor or secretory) limb and a central (ganglionic) portion. The last may be located within the cerebrospinal axis (cerebrospinal reflex) or within the vegetative nervous system (axon reflex).

The afferent limb of this reflex arc is made up of fibers of the ophthalmic division of the trigeminus, which are distributed to all the tissues of the bulbus. Sensory stimuli, arising in any part of the eye, are conveyed by these fibers to ganglion cells of the ciliary ganglion.¹⁰

⁹ As early as 1864 the great physiologist F Goltz demonstrated a tone in the veins which was dominated by nerves.

¹⁰ The impulses travel thence to the gasserian ganglion, to the nuclei of the trigeminus and then to the thalamus (of the same and, mainly, of the opposite side). Finally, through interpolation of thalamic neurons, the impulses reach the cerebral cortex (somatic area in the upper part of the parietal lobe).

As was pointed out in the first article,^{1a} neither within the uveal tract nor in the ciliary processes can ganglion cells be found. In my opinion the ciliary ganglion, along with the numerous nerve fibers within the eye, is to be considered as one unit. The ciliary ganglion embryologically a derivative of the gasserian ganglion (Keibel and Mall¹¹), is a sensory organ and the only one in the eyeball since nowhere else can sensory terminations be detected within the bulbus (Stohr¹²). This ganglion is the center for all the nerve impulses arising within the eye. It represents the central portion of the reflex arc under discussion.

It is essential to recall that the ciliary ganglion has the following connections: (1) With the sympathetic nervous system through its short root. By this path impulses are carried to the sphincter iridis and to the ciliary muscle. The radix brevis is an efferent, visceromotor bundle. (2) With the sympathetic nervous system, through its sympathetic root. These fibers derive immediately from the cavernous and the internal carotid plexus but they originate in the ganglion cervicale supremum¹³ and the centrum ciliospinale (Budge¹⁴) in the spinal cord (at the level of the sixth cervical to the third thoracic segment). These too, are efferent fibers, innervating the dilator iridis, Muller's muscle and the vessels and capillaries of the eye.

The ciliary ganglion being a part of the brain, shifted to the periphery by migration from the gasserian ganglion during embryonic life, the reflex arc is therefore, a cerebral reflex.

Failure in the maintenance of the normal intraocular pressure may result from irritation of any one of the three components of this reflex arc.

Clinical Aspect—Increased intraocular pressure may be due to the following factors:

I Irritation of the Afferent Limb

A Diseases of the eyeball

1 Cornea (a) Keratitis punctata superficialis

In the second article^{1b} I mentioned

11 Keibel, F., and Mall, F. P. Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, p. 118.

12 Stohr, P., Jr. Mikroskopische Anatomie des vegetativen Nervensystems, Berlin, Julius Springer, 1928, p. 211.

13 Attention has not been paid in the ophthalmologic literature to the fact that the ganglion cervicale supremum is closely connected with an important blood pressure-controlling structure, the carotid sinus. A sudden rise of blood pressure, with its deleterious effect on the eye may on occasion be related to the carotid sinus. The role of the ganglion cervicale supremum in epinephrine mydriasis has been pointed out by me.¹⁶

14 Budge, J. Ueber die Bewegungen der Iris. Braunschweig, Fr. Vieweg u. Sohn, 1855.

a case under my observation in which the condition started with small, painful erosions, followed by acute glaucoma (b) Keratitis parenchymatosa, with episodes of high intraocular pressure (c) Synechia anteriores, particularly with complete adhesion of the pupillary part of the iris to the cornea.

It might be of interest to mention the "hypertonic reaction." After puncture of the anterior chamber in animals, the intraocular pressure starts to rise slowly and later increases rapidly up to 40 or 50 mm. of mercury, after oscillations the pressure returns to its normal level. Similar oscillations may be observed in patients.

- 2 Sclera Scleritis profunda
 - 3 Iris (a) Iritis serosa (glaucomatosa), (b) synechia posteriores, (c) cyclitis
 - 4 Lens (a) Cataracta traumatica, (b) cataracta senilis intumescens, (c) luxatio traumatica
 - 5 Retina (a) Retinitis pigmentosa
 - B Involvement of the veins with passive hyperemia of the eye
 - 1 Cardiac failure
 - 2 Engorgement of the veins due to local inflammation with occlusion of certain venous branches (tenonitis)
 - 3 Thrombosis of venae vorticosae
 - 4 Periphlebitis in the vicinity of the eyeball
 - 5 Perforation of the internal carotid artery into the cavernous sinus
 - 6 Pressure of intraocular tumors on veins
 - 7 Thrombosis of the venae centralis retinae
- Undoubtedly, the mechanical blockade to the venous flow is important. However, the cause of the secondary "inflammatory" changes with high intraocular pressure which may develop, without any signs of common inflammation, is entirely unknown. In the course of large intraocular hemorrhages, the intraocular pressure usually does not rise. Nor is the destruction of the retina as a sequel of occlusion of the arteria centralis retinae complicated with glaucoma. I may refer, with due caution, to this reflex. It may be of interest to recall that relief of pain and of congestion of the eye may sometimes be obtained by application of leeches to the temple, by withdrawal of blood and by use of cathartics. Note-worthy, as I said in the first article¹¹

is the intimate connection of the venous flow in the bulbus with many large venous plexuses in the vicinity (the reason for cauterization of the venous plexus at the middle turbinate, once advocated for treatment of glaucoma, can now be better understood)

8 Mydriasis, with pressure on the canal of Schlemm, and secondary venous engorgement Severance of the afferent limb (iridectomy, Elliot's operation, cyclodialysis) will therefore lower the intraocular pressure¹⁵

II Irritation of the Efferent Limb

- 1 Miotics, stimulating the parasympathetic portion of the reflex arc
- 2 Ergotamine, paralyzing the sympathetic nerves, an effect which is equivalent to stimulation of the antagonist
- 3 Epinephrine, acting as a stimulus to the sympathetic fibers This effect is at first glance confusing It proves, nevertheless, to be helpful in certain cases, not in those of the acute inflammatory type¹⁶

III Irritation of Central Part of the Reflex Arc

1 Ciliary ganglion

Of great interest from the point of view of this study is herpes zoster ophthalmicus Aside from the well known involvement of the cornea, which may include all the tissues of the eye, there may be unilateral mydriasis, with lack of response to light The tone of the bulbus is often lowered (Meller¹⁷), but in 1 interesting case (Urrets Zavalia¹⁸), increase in intraocular pressure, without any sign of obstruction of the angle, was the initial sign The syndrome of unilateral mydriasis, with absence of reaction to light, and high intraocular pressure is striking and reminiscent of acute

¹⁵ Removal of the ganglion cervicale supremum (Abadie, C Bull Soc d'opt de Paris, 1927, no 9, p 528 Lindsay, R R Neuro-Ophthalmology, St Louis, C V Mosby Company, 1941, p 400) or roentgen irradiation (Thiel, R Klin Monatsbl f Augenh **82** 1909, 1929) would eliminate certain sympathetic influences It could facilitate the action of epinephrine (Hess¹⁶)—nothing more It will soon be seen that a curative effect on glaucoma cannot be anticipated from this operation

¹⁶ Hess, L Epinephrine Mydriasis, Arch Ophth **30** 194 (Aug) 1943, footnote 1a

¹⁷ Meller, J Ztschr f Augenh **43** 450, 1920

¹⁸ Urrets Zavalia Arch de oftal de Buenos Aires **1** 156, 1926

glaucoma The primary site of herpes zoster ophthalmicus is the central portion of the sensory pathway of the eye, the gasserian ganglion But in addition André-Thomas and Heuyer¹⁹ demonstrated by microscopic studies severe active hyperemia and inflammation of the ciliary ganglion, i e, of the central portion of the reflex arc I feel justified in tracing the abnormal intraocular pressure associated with herpes zoster ophthalmicus to the involvement of the ganglion ciliare

THE SECOND (DIENCEPHALIC) REFLEX ARC

By means of the regulatory mechanism outlined in the preceding section, all of the clinical signs of glaucoma in the affected eyeball can be accounted for Here, one is confronted with an important question, for it is not one eye, but in most cases both eyes, which are involved sooner or later With chronic glaucoma, even in the "normal" eye, the intraocular pressure may rise at night and the anterior chamber may be found to be shallow, the normal intraocular pressure being maintained, as has been mentioned, at constant level with but little oscillation, apparently owing to the activity of a regulating nerve center When in cases of chronic glaucoma the function of this center is disturbed and the fluctuations of the intraocular pressure are pronounced, the possibility of a central nervous disturbance (anatomic or functional) must be considered This concept seems to be confirmed by clinical and experimental facts

Weekers²⁰ noted a rise in intraocular pressure in both eyes after cauterization of one eye According to Thiel,²¹ when the intraocular pressure falls in the injured eye, it drops for several days in the normal eye Vom Hofe²² observed bilateral lowering of the pressure after injection of a small amount of saline solution into one vitreous body

Interesting are the studies by Kahler and von Sallmann²³ on patients with cerebral hemiplegia On the paralyzed side the intraocular pressure was lowered

¹⁹ André-Thomas and Heuyer Rev neurol **381**, 1912 André-Thomas Le zona, Arch Neurol & Psychiat **27** 216 (Jan) 1932

²⁰ Weekers, L J de neurol **25** 778, 1925, Arch Ophth **41** 641, 1924

²¹ Thiel, R, in Schieck, F, and Bruckner, A Kurzes Handbuch der Ophthalmology, Berlin, Julius Springer, 1931, vol 4

²² vom Hofe, H Arch f Augenh **102** 315, 1929

²³ Kahler, H and von Sallmann, L Wien klin Wehnschr **36** 883, 1923

The occurrence of glaucoma after emotion has been noticed (Schoenbeig²⁴) Of importance are the pupillographic studies of Lowenstein and Schoenberg, demonstrating pupillary reactions of the "unaffected" eye in cases of unilateral glaucoma Stimulation of the sympathetic trunk of one side gives rise to bilaterally increased intraocular pressure

Papilian and Cruceanu²⁵ removed one hemisphere of the cerebellum in rabbits On the side of operation the intraocular pressure remained unchanged or was slightly lowered, on the opposite side it was elevated

It is in keeping with the physiology of today to search for a cerebral representation of any vegetative function As was suggested in the second article, the subthalamic, diencephalic center of the vegetative nervous system (Karplus and Kreidl²) would provide the possibility of a bilateral nerve control of the eye Stimulation of this center results in the acute experiment in protrusion of the bulbus, maximum mydriasis,

widening of the palpebral fissure, lacrimation and pain—i.e., all the nervous signs associated with glaucoma The pathways connecting this center with the nerves of the eye are the peduncles, the upper thoracic portion of the spinal cord and the centrum ciliospinale (Budge) Thence, the impulses spread to the ganglion cervicale supremum, to the cavernous and carotid plexuses and, finally, to the ciliary ganglion

THIRD (CORTICAL) REFLEX ARC

Extensive clinical studies provided evidence (Hess and Faltitschek²⁶ that there are no vegetative centers in the cortex Marburg²⁷ stated the belief that the subthalamic centers extend far upward to the medial aspect of the thalamus The latter is connected with the cortex by the corticothalamic fibers It is possible that the thalamus responds thus to cortical impulses (anxiety) and that through the thalamus the hypothalamic organ eventually becomes activated

15 Kenwood Street, Brookline, Mass

24 Schoenberg, M J Role of States of Anxiety in Pathogenesis of Primary Glaucoma, Arch Ophth **23** 76 (Jan) 1940

25 Papilian, V., and Cruceanu, H Compt rend Soc de biol **92** 1081, 1925

26 Hess, L, and Faltitschek, J Wien klin Wchnschr **43** 488, 1930

27 Marburg, O Verhandl d deutsch Gesellsch f Nervenärzte **18** 208, 1929

OPHTHALMOLOGIC FEATURES OF INTRACRANIAL CHORDOMA AND ALLIED TUMORS OF THE CLIVUS

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Intracranial chordoma and allied tumors of the clivus are of significance to the ophthalmologist, who may be the first to see the patient, since diplopia and visual disturbances occur in over a third of the cases and may, together with headache, be the only symptoms. In 1 case reported in the literature¹ muscle exercises were given before the true nature of the lesion was determined. The age incidence and the sequence of the symptoms may suggest that the tumor is chordoma, a diagnosis which can be further verified by roentgenographic and encephalographic studies.

That this suspicion may be of value to the neurosurgeon is easily understandable when it is realized (1) that tumors of this type are almost invariably fatal if left alone and (2) that surgical intervention in selected cases offers the only hope. If the surgeon suspects chordoma, he should not attempt complete removal but, rather, should employ suction of the gelatinous or mucinous content of the tumor, which, if successful will relieve pressure symptoms for a few years. If complete removal is attempted, death is likely to result.

A chordoma is a neoplasm arising from embryonic rests of the chorda dorsalis, a specific embryonal tissue about which the spinal column develops. As the base of the skull is molded, the posterior end of the cranial part of the chorda is forced backward and dorsally so that it lies on the occipital plate in a dorsal groove anterior to the foramen magnum. This embryonal tissue persists in infants in the centers of the intervertebral disks and in the coccyx, as well as at the base of the skull. Virchow² (1856) recorded the first description of a chordoma. In 1857, because of the physaliphorous nature of

the tumor cells and because of his belief that they were of cartilaginous origin, he named the tumor ecchordosis physaliphora spheno-occipitalis. Muller³ (1858) first stated that the tumor originated from embryonic rests of the chorda dorsalis. Ribbert,⁴ in 1894, named the tumor chordoma. In 1897 Nebelthau⁵ identified glycogen in the cytoplasmic vacuoles. The first case of symptomatic chordoma was reported by Klebs⁶ in 1864. Grahl⁷ studied the first spheno-occipital chordoma of clinical importance. Hass,⁸ in 1934, published an excellent review of the literature on chordoma of the cranium and the cervical portion of the spine. The completeness of his bibliography makes it necessary to comment on reports made only after that date.

In this paper interest is directed only to spheno-occipital tumors and not to growths in the sacrococcygeal or vertebral area or in the region of the jaw. To date less than 100 cases of spheno-occipital chordoma have been reported. The benign form is of no clinical importance. The so-called malignant form is a slow, expansive growth traversed by fibrous septums, between which is a sparsely cellular tissue composed largely of an intracellular matrix of gelatinous or mucinous character. The early structure resembles hyaline cartilage but is without intercellular substance. The cells are round large, vacuolated and hyperchromatic and may resem-

3 Muller, H. Ueber das Vorkommen von Resten der Chorda dorsalis bei Menschen nach der Geburt und über ihr Verhältniss zu den Gallertgeschwulsten am Clivus, *Ztschr f rat Med* 2: 202, 1858.

4 Ribbert, H. Ueber die Ecchondrosis physaliphora spheno-occipitalis, *Centralbl f allg Path u path Anat* 5: 457, 1894.

5 Nebelthau, L A. Ueber die Gallertgeschwulste am Clivus Blumenbachii, *Inaug Dissert*, Marburg, 1897.

6 Klebs, E. Ein Fall von Ecchondrosis spheno-occipitalis amylacea, *Virchows Arch f path Anat* 31: 396, 1864.

7 Grahl, O. Eine Ecchondrosis physaliphora spheno-occipitalis ungewöhnlichen Umfangs mit interessanten klinischen Folgen, *Inaug Dissert*, Göttingen, W F Kaestner, 1903.

8 Hass, G M. Chordomas of the Cranium and Cervical Portion of the Spine. Review of the Literature with Report of a Case, *Arch Neurol & Psychiat* 32: 300 (Aug) 1934.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Nov 20, 1944.

1 Carmichael, F A, Helwig, F C, and Wheeler, J H. Cranial Chordoma. Report of a Case in Which Surgical Intervention Was Successful, *Am J Surg* 55: 583 (March) 1942.

2 Virchow, R. Ueber die Kretinen-Physiognomie, *Verhandl d phys-med Gesellsch* 8: 24, 1857, Untersuchungen über die Entwicklung des Schadelgrundes, Berlin, G Reimer 1857, p 51.

ble epithelium (fig 1). The numerous variations in cell form, the occurrence of glandular alveolar structure, the morphology and staining reactions of the fibrils, the relation to cartilage and the taking of a red stain for glycogen are characteristic. The red stain obtained with carmine does not necessarily indicate glycogen, as the latter is soluble in water and is thus dissolved out in the solution of formaldehyde.⁹ Ewing, however, stated that positive identification is not readily accomplished, as there is a close similarity between chordoma and myxochondroma. Because some of the cases in the literature of so-called chordoma are more than likely cases of myxochondroma I have included the latter in this discussion for clinically the two tumors are indistinguishable except for the more frequent occurrence of calcification in chordoma.

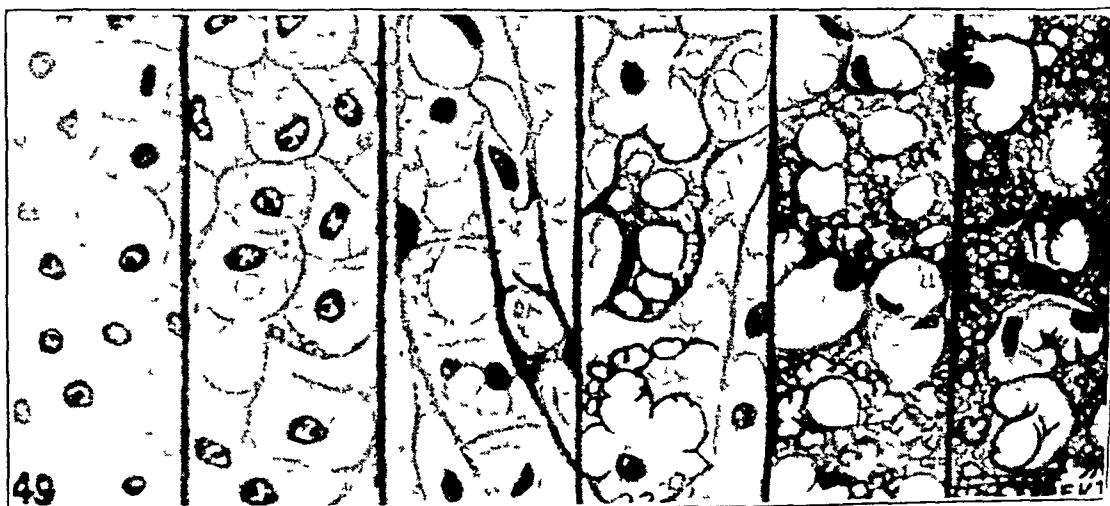


Fig 1.—Transitions from the well preserved epithelioid tumor cells of chordoma through the physaliferous and signet-ring type of cell to extensive mucinoid degeneration (from Harvey, W F, and Dawson, E K Chordoma, Edinburgh M J 48 713, 1941)

The majority of the tumors first cause symptoms in the third or fourth decade of life—the average age being 36 years. The first symptom can occur, however, at any age from birth to 82 years. These tumors are found more frequently in males the incidence being about 60 per cent. Characteristically they are located in the median line beneath the dura. Progression anteriorly is characterized by erosion of the sella turcica and compression of the optic chiasm. The osseous walls of the orbital cavities may be involved.

SYMPTOMS

The four most common symptoms of tumors of the clivus are headache, visual disturbances,

nasal obstruction (from ventral extension of the tumor in the direction of the nasopharynx) and pain in the neck. The headaches are of increasing severity, with temporary periods of relief, and are referred to the frontal or the occipital region. Visual disturbances are the result of compression of the optic chiasm or of the sixth nerve.

Although the tumors are typically in the midline beneath the pons, there is a pronounced tendency for involvement of the cranial nerves to be unilateral, and even if the involvement is bilateral, it is more complete or widespread on one side than on the other. In 13 cases reported in the literature there were choked disks and in 10 optic nerve atrophy. Various defects in the visual fields simulated those caused by primary tumor of the hypophysis but in the differential

diagnosis there was lack of evidence of a functional disturbance of the hypophysis and headache preceded changes in the visual fields, this is a reversal of the symptoms of tumor of the pituitary. Blurred vision, diplopia, internal strabismus, altered pupillary reaction, dilatation of the pupils, anisocoria and partial or complete ophthalmoplegia were a few of the various manifestations encountered on examination. Paresis of the abducens nerve occurred in 34 cases and was the most frequent symptom, it usually preceded the onset of paralysis of other ocular nerves. In the early stages paresis of the abducens nerve was predominantly on the left side, although in the late stages it was bilateral. Similarly, paralysis of the third and fourth nerves on the left side was more common than bilateral involvement. In almost every instance in which the facial nerve was disturbed the sixth nerve

⁹ Adson, A W, Kernohan J W, and Woltman H W. Cranial and Cervical Chordomas. A Clinical and Histologic Study, Arch Neurol & Psychiat **23** 247 (Feb.) 1935

was also involved. Practically any cranial nerve could be involved with limited frequency.

Second in importance to involvement of the cranial nerves was the compression of the brain stem and the spinal cord in the region of the foramen magnum. Hemiparesis on the left side occurred in 6 of 7 cases. If the tumor was pushed through the foramen magnum, pain in the neck, which was accentuated by motion of the head, occurred. Van Wagenen¹⁰ suggested that the frequency of symptoms and the onset are an aid in diagnosis. These symptoms in their order of frequency are as follows: palsies of the oculomotor nerves with palsy of the sixth nerve as the most common; bilateral involvement of

characteristic V-shaped notch in the basilar plate as an almost certain sign. A ventriculogram may show an elevated third ventricle.

The average duration of illness after involvement of the cranial nerves is about three years. However, cases in which the course was of eight

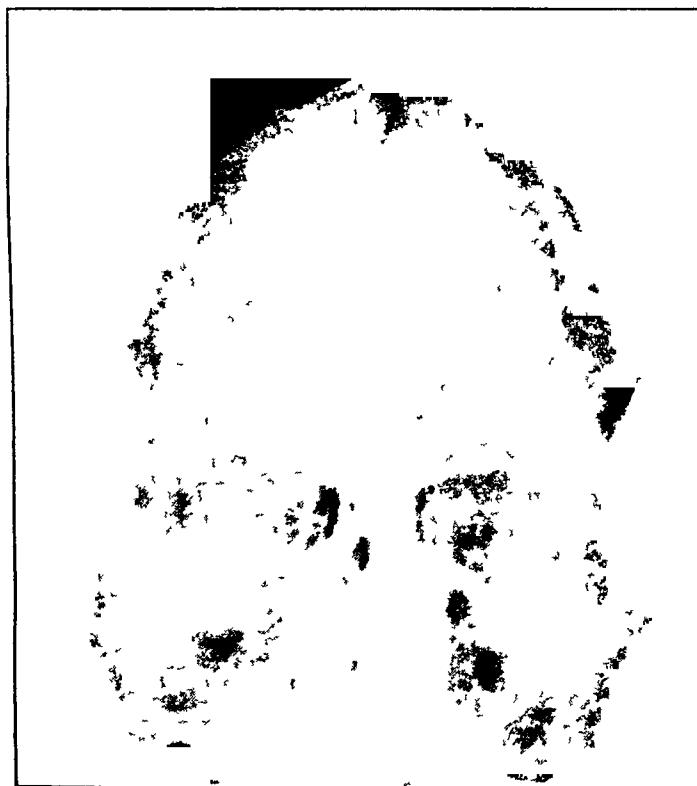


Fig. 2.—Roentgenogram showing calcific flecks and increased density on the left side opposite the area of the sella turcica.

cranial nerves, symptoms of intracranial pressure, and involvement of the optic nerve.

Machulko-Horbatzewitsch and Rochlin¹¹ stated, in another way, that a typical course is characterized by involvement of the sixth cranial nerve followed by bulbar implication.

A roentgenogram indicates a destructive, non-productive lesion of bone. Sosman, in a personal communication to Van Wagenen, pointed out a

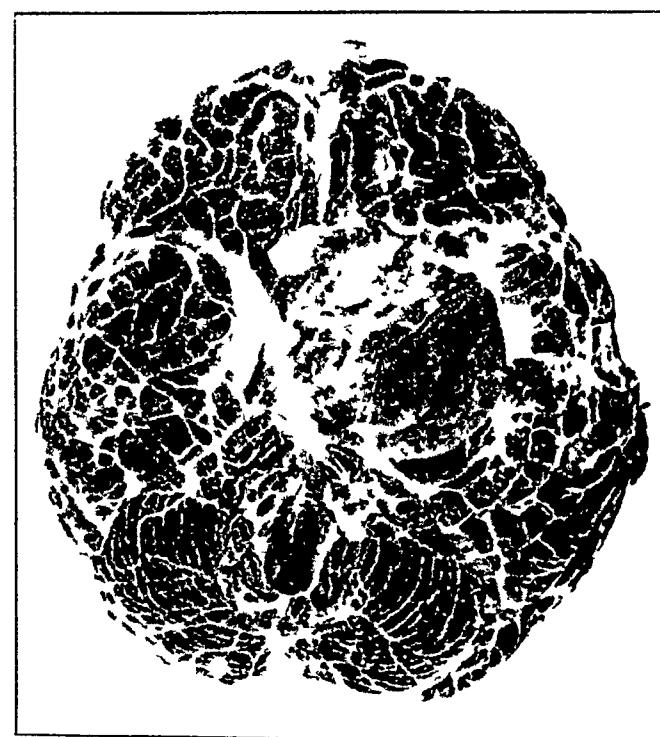


Fig. 3.—Under surface of the brain, showing the location of the myxochondroma.



Fig. 4.—Tumor mass, 7 by 6.5 by 6 cm. The rule is in centimeters.

months to eighteen years' duration have been recorded.

In the differential diagnosis the following possibilities should be considered: tumor of the fourth ventricle, meningioma, tumor of the cerebellopontile angle, infiltration tumor of the pons (glioma), and vascular lesions of the pons.

¹⁰ Van Wagenen, W. P. Chordoblastoma of the Basilar Plate of the Skull and Eccordosis Physaliphora Spheno-Occipitalis. Suggestions for Diagnosis and Surgical Treatment, Arch Neurol & Psychiat **34**: 548 (Sept.) 1935.

¹¹ Machulko-Horbatzewitsch, G. S. and Rochlin, I. L. Klinik Pathomorphologie und Histogenese der Chordome, Arch f Psychiat **89**: 222, 1930.

REPORT OF CASES

CASE 1—R W, a youth aged 20, was seen on March 18, 1941, through permission of Dr Carl A Peterson. His chief complaint was turning in of the left eye for the past ten months. The patient had previously been examined at St Vincent's Hospital, five months after occurrence of this symptom. Complete examination, including roentgenographic study of the skull, revealed no abnormality at that time.

When the patient was first seen at the New York Post-Graduate Hospital, his vision was 20/20 in the right eye and 20/25 in the left eye, no change in the fundi or visual fields was noted. Paralysis of the left lateral rectus muscle was present.

light, no perception of light was present, and the fundus showed primary optic nerve atrophy.

General examination gave normal results except for paralysis of the left lateral rectus muscle and atrophy of the left optic nerve. The deep reflexes were greater on the right side, and the Babinski sign was present on that side. Sensory examination revealed nothing abnormal. A roentgenogram taken at this time showed an area of increased density, nearly 2 inches (5 cm) in diameter, with numerous calcific flecks on the left side, opposite and extending somewhat posterior to the sella turcica (fig 2).

An electroencephalogram indicated abnormal activity over both frontal lobes and the left occipital cortical

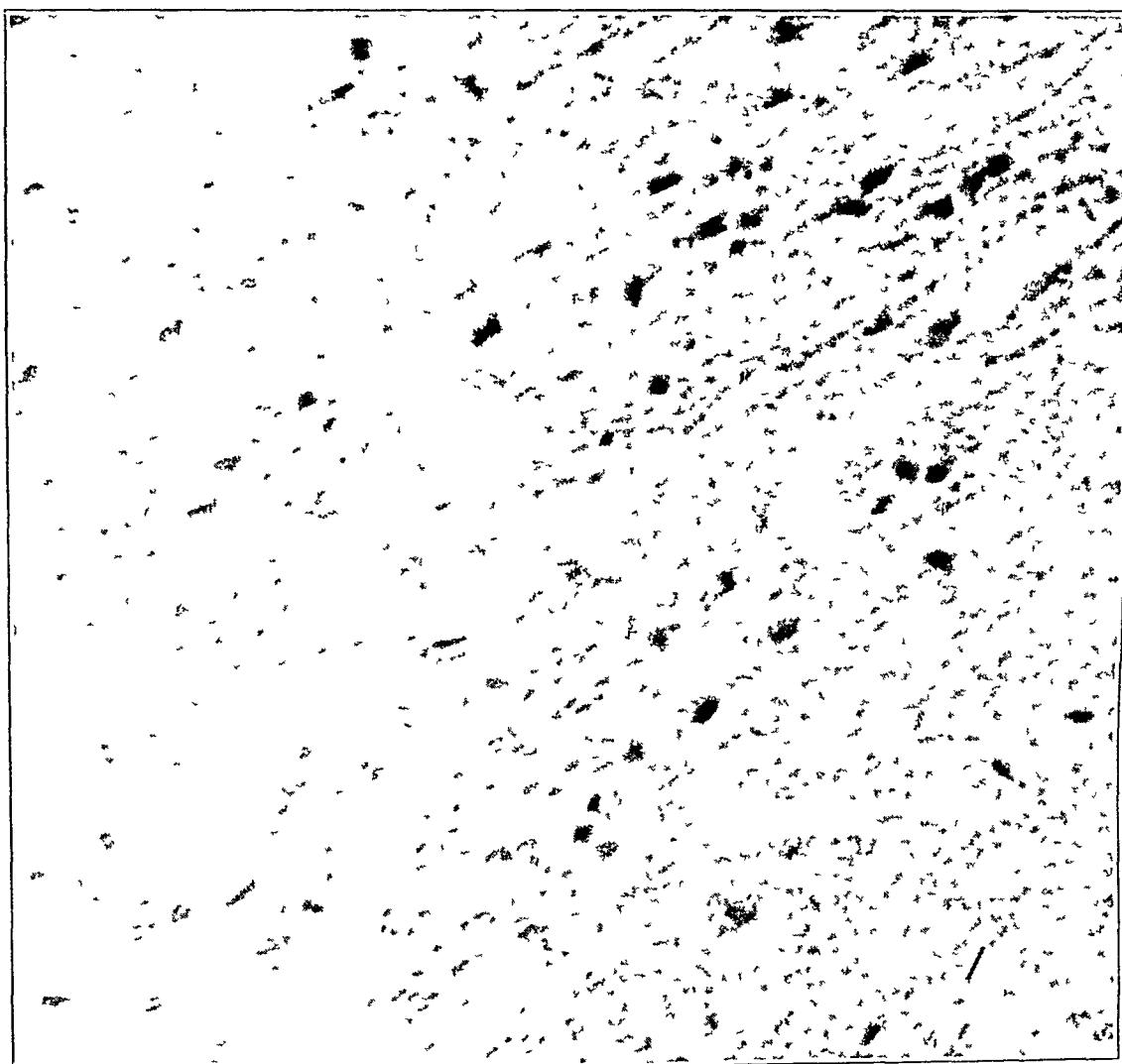


Fig 5.—Photomicrograph of basophilic myxomatous tissue, with many moderately large, round, oval and stellate cells.

He was not seen again until Sept 15, 1942. At that time he gave a history of difficulty in facial expression for four months. For the past month there had been weakness of his right arm. Headache had started about one year previously, and impairment of vision in his left eye had occurred about six months before. Since the onset of decreased vision in his left eye headache has ceased.

His right pupil was 5 mm in diameter and reacted normally. There was loss of the temporal field of the right eye suggesting that homonymous hemianopsia in the right eye had probably preceded the present state. His left pupil was 6 mm in diameter and was fixed to

area, with the abnormality more prominent over the latter region. A lesion in this area was suspected.

On Oct 1, 1942 a decompression was done and the left middle fossa explored, a tumor was felt in the left temporal region, but it could not be exposed. The patient died the next day.

Diagnosis at necropsy was chondroma of the left spheno-occipital synostosis, with hemorrhage into the left lateral ventricle, the left cortex and the basal ganglia (postoperative). When the brain was removed, a tumor was uncovered, firmly attached to and apparently arising from the junction of the sphenoid and the occipital bone on the left side, between the

sella turcica and the foramen magnum. It measured 7 by 6.5 by 6 cm (figs 3 and 4) and arose 1 cm to the left of the midline. From there it extended laterally into the left middle fossa, stretching and compressing the left optic nerve and compressing the overlying temporal and parietal lobes on the left side. The tumor was below the dura at the base of the skull. It was firm and, on section, was observed to be composed of grayish white, semiliquid, gelatinous tissue, with large areas of bone formation. Microscopically the tumor consisted of basophilic myxomatous tissue, in which there were many moderately large, round, oval and stellate cells (fig 5). These cells had moderately dark, round and oval nuclei, with delicate chromatin network

C. F., a woman aged 29, single, for the past two years had had diplopia and frequent headaches, particularly in the back of the head.

Examination on June 29, 1942 revealed that the pupils reacted to light, in accommodation and consensually. The left lateral rectus muscle was paralyzed. There was external ophthalmoplegia on the right side, due to involvement of the third nerve. Dr. Lowenstein made the following report. The deep reflexes on the right side were greater than those on the left, a questionable Babinski sign was elicited on the right side. The fundi and the visual fields were normal.

A ventriculogram made later revealed a concentric defect on the under surface of the third ventricle.

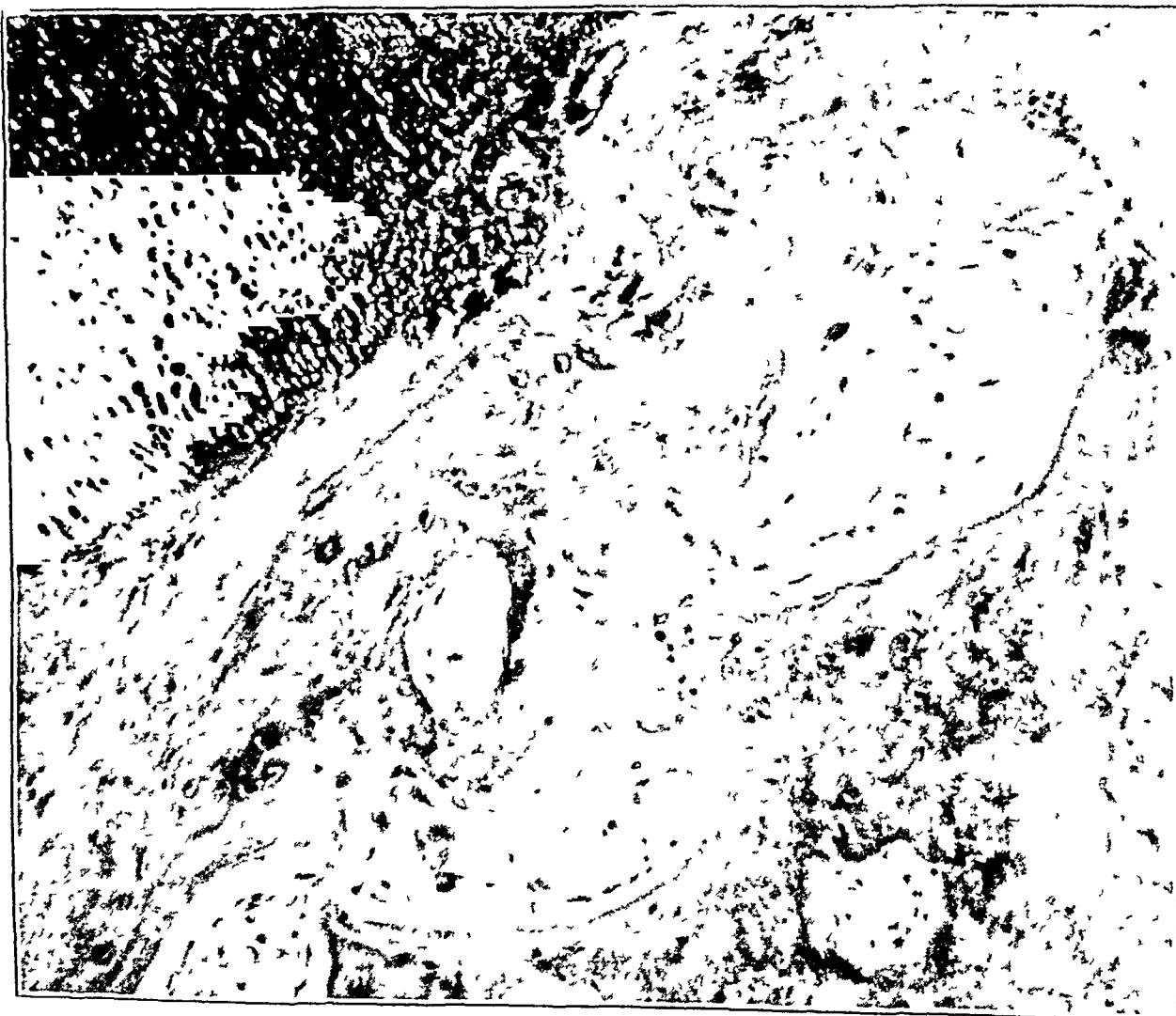


Fig. 6.—Photomicrograph of areas of bone and cartilage formation in the tumor.

Large areas of bone and cartilage formation were present (fig 6). There was a limiting capsule of dense fibrous tissue. Histologically one cannot be certain whether this tumor was a chordoma or a chondroma. The pathologists consulted expressed a preference for the diagnosis of chondroma.

CASE 2—This case was observed through permission of Dr. Otto Lowenstein. The correct preoperative diagnosis was made by Dr. E. D. Friedman, who will report this case in detail at a later date. I refer to it here because the characteristic paralysis of the left lateral rectus muscle was an early sign and because postoperative histologic study verified the diagnosis of chordoma.

This corresponded with the position of the tumor mass, which was aspirated at operation, on Oct. 20, 1943. The histologic diagnosis was chordoma.

At the time of writing the right pupil was dilated (6 mm in diameter) and did not react to light. Ptosis was present on the right side. The left pupil was 3 mm in diameter and reacted to light. The patient held her head to the right because of the paralysis of the left lateral rectus muscle.

CONCLUSION

If the ophthalmologist suspects that an intracranial tumor is a chordoma, his impression

should be conveyed to the neurosurgeon in order that the handling of the case may be materially altered.

Unexplained paralysis of the lateral rectus muscle more frequently the muscle on the left side, in a patient in his thirties with progression to chiasmic signs, headache preceding defects of the visual fields and no evidence of disorder of the pituitary should suggest chordoma. Roentgenograms, encephalograms and ventriculograms, as well as subsequent bulbar involvement, may add corroborating evidence.

108 East Sixty-Sixth Street

DISCUSSION

DR E D FRIEDMAN, New York. I might amplify the report that Dr Givner has already given of the second case. A woman aged 30 was admitted to the Bellevue Hospital on July 10, 1942. Her chief complaints were double vision, with strabismus of four or five years' duration, mild headache, urinary urgency (for many years) and occasional episodes of loss of equilibrium, with a tendency to fall to the left. She presented a complete lesion of the right third nerve (for the past year), palsy of the left external rectus muscle (for five years) and normal disks. The rest of the neurologic status was normal, and the serologic reactions were negative.

The results of roentgenologic studies including encephalographic examination, were considered negative for tumor but were later reinterpreted, in view of the course of events. I shall demonstrate a few abnormalities which were present in the first roentgenograms but which my colleagues and I failed to evaluate properly.

The diagnosis on her discharge from the hospital was chronic encephalitis or syphilis. Nine months later she was readmitted because of increasing headache and dizziness, bouts of nausea and vomiting, weakness of the right arm and leg, numbness and tingling on the right side and difficulty in urination. Her general medical status was normal. The blood pressure readings were 130 systolic and 90 diastolic. No bruit was heard over the head.

Neurologic examination showed that visual acuity was somewhat impaired, but the fields were normal, and there was no papilledema. There was a lesion of the right third nerve, with a dilated sluggish pupil. The left pupil was normal. There were weakness of the left external rectus muscle and slight weakness of the right side of the face. The tongue was deviated to the right. There was right hemiparesis with increased tone and dragging of the right foot. Some cerebellar signs were present on the right side, with a tendency to fall to the right. The deep reflexes were more active on the right. All the abdominal reflexes were absent. Ankle clonus

and the Babinski sign were elicited on the right side. Mild hypalgesia was present on the same side.

The urine was normal. Examination of the blood showed mild secondary anemia. The Wassermann reaction of the blood was negative. Blood chemistry was normal. The spinal fluid was under normal pressure, the total protein measured 100 mg per hundred cubic centimeters. The Pandy reaction was positive and the Wassermann reaction negative.

We then reviewed the roentgenograms and encephalograms taken in 1942. In the lateral view of the skull, the dorsum sellae was eroded, and there seemed to be a calcified mass behind the sella in the region of the clivus. The first pneumoencephalogram showed a normal ventricular system with no evidence of dilatation. In the encephalograms taken about nine months later a striking change was evident. The vestibular system had become dilated, the third ventricle, instead of being in the normal position, had been lifted up and was dilated and globular.

On the basis of the clinical history, the encephalographic findings and the simple roentgenograms of the skull, we ventured the diagnosis of chordoma. Aneurysm and meningioma at the base were also considered as possibilities but I thought that aneurysm could be excluded by the absence of signs of involvement of the fifth nerve and by the presence of bilateral ophthalmoplegia.

Craniotomy was carried out by Dr Joseph E. J. King on Oct 20, 1943. Through a transcallosal approach he exposed a tumor which protruded upward through the floor of the third ventricle. Examination of portions of this tumor showed hard calcified nodules. The pathologic diagnosis was chordoma.

As Dr Givner has indicated, chordoma has its origin from the primitive notochord. The favorite sites are the clivus and the sacrum; the tumor is usually locally invasive but does not metastasize. There are no endocrine stigmas, such as one encounters in primary growths of the pituitary, and the symptoms indicate bilaterality. The ophthalmologic signs in this case appeared first on the left and later on the right, this is characteristic. There is usually a history of long illness but papilledema is not present. In this respect chordoma in this region behaves like the so-called Schmincke tumor, which produces multiple cranial nerve palsies, owing to invasion of the base of the skull, but does not act like an intracranial tumor, which usually gives rise to papilledema.

Chordoma must be distinguished from aneurysm, the symptoms of which are seldom bilateral and are accompanied with signs referable to the fifth nerve, as has already been indicated.

I have now had the privilege of observing 3 cases of intracranial chordoma, the symptoms in all being somewhat similar. One makes the

diagnosis with hesitation but it is occasionally a good guess

DR JOSEPH LAVAL, New York Will Dr Friedman say more about the differentiation of the early stages of chordoma and meningioma?

DR E D FRIEDMAN, New York I may simply say that we missed the diagnosis during our first observation of the case. We did not know what we were dealing with, we thought of syphilis but could not prove the diagnosis,

we thought of chronic encephalitis, a diagnosis which is always dangerous and which the Germans call a "diagnosis of embarrassment." From the subsequent course of events, we felt that the case was one of a midline lesion exerting pressure on both sides. We were not inclined to the diagnosis of meningioma, meningioma usually produces unilateral signs. The long history, the bilaterality of signs and the roentgenographic evidence led us to favor the diagnosis of chordoma.

USE OF TRONCOSO'S MAGNESIUM IMPLANT IN CYCLODIALYSIS FOR RELIEF OF GLAUCOMA

OBSERVATIONS IN TWO CASES

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JOHANNESBURG, SOUTH AFRICA

The implantation of a strip of magnesium along the spatula tract in cyclodialysis is a modification suggested by Uribe Troncoso.¹ Because one is often forced to resort to cyclodialysis one always feels that it is but a temporary measure. I wish to report on the postoperative course in 2 cases in which moderately severe reactions took place. In both cases the exact technic as described by Troncoso was followed except that a single, 6 by 1.5 mm strip of magnesium was employed. This is less than the amount used by Troncoso.

Mr F R, aged 62 years, had a blind right eye due to thrombosis of the central retinal vein. The eye was

anterior chamber. The metal commenced to bubble immediately on insertion, and after twelve hours the whole anterior chamber was filled with gas. The cornea, however, remained clear in spite of a pressure of 50 mm of mercury (Schiøtz). The iris was moist, and there was a fairly large subconjunctival bubble of gas. Because of the pain and because an obstruction to the escape of gas was thought to exist, a thin hypodermic needle was inserted through the cornea, the escape of the gas could be heard. Before deflation the eye was tympanitic when touched with the needle point. After deflation the anterior chamber immediately filled with a blood-stained fluid, and the pain subsided at once. This procedure had to be repeated daily for six days. After this there were a large bubble of gas in the anterior chamber and a similar bubble under the conjunctiva for three or four days.

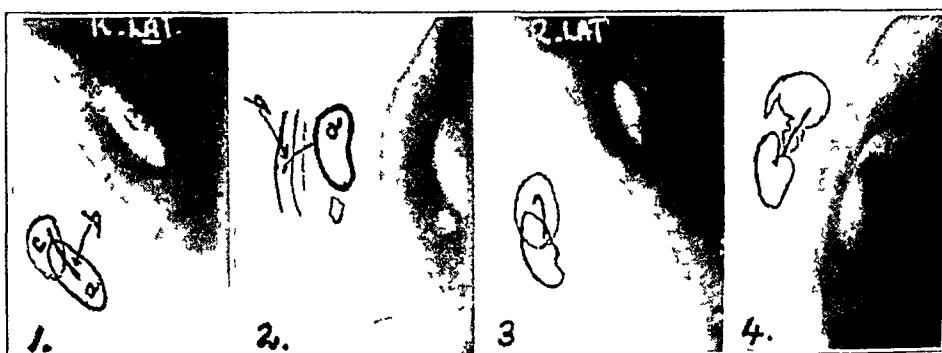


Fig 1—1. Roentgenogram taken in Vogt's position, with the film pressed in between the nose and the eye. A soft tissue exposure is made from the lateral side. This shows (a) the anterior chamber of the eye filled with gas, (b) a thin dark line which is caused by the piece of magnesium, and (c) a subconjunctival bubble of gas.

2, roentgenogram taken in Clark's position, with the film pressed in between the lower edge of the orbital rim and the eye. A soft tissue exposure is made from a subconjunctival bubble of gas and (b) the shadow of the magnesium implant.

3 and 4, roentgenograms taken in Vogt's and Clark's positions, respectively, two days after the roentgenograms 1 and 2. The shadow of the magnesium implant is more indefinite (arrow).

glaucomatous, with an intraocular pressure of 54 mm of mercury (Schiøtz). He refused enucleation, and it was decided to do an operation for implantation of magnesium in an attempt to retain the bulbus oculi. The strip was not inserted opposite 12 o'clock on the limbus because gonioscopic examination revealed engorgement of the vessels over the peripheral fold of the iris and a patch of enlarged capillaries on the surface of the adjacent ciliary body in the vertical meridian. In this congested patch capillary loops extended into the pectinate meshes of the uveal trabecula. The congested canal of Schlemm was visible as a pinkish line along the entire circumference of the angle. To avoid this area of engorged vessels, the magnesium was implanted opposite 10 o'clock, in the angle of the

Several interesting observations are worthy of record in this case.

1 Before the operation the cornea was hazy at an intraocular pressure of 54 mm of mercury (Schiøtz), while the cornea was absolutely clear when the anterior chamber was full of gas, although the pressure varied from 49 to 55 mm of mercury (Schiøtz). The haziness may be explained by the presence of corneal edema, due to aqueous being forced into the stroma through minute openings in the layer of Descemet.

2 On cocaineization, prior to insertion of the hypodermic needle for escape of the gas, the cornea became insensitive within the normal period, but the iris remained intensely sensitive to being touched with the needle. This shows

¹ Uribe Troncoso, M. Cyclodialysis with Insertion of a Metal Implant in the Treatment of Glaucoma, Arch Ophth 23:270 (Feb) 1940, Tr Sect Ophth, A M A, 1939, p 389.

that in routine cocainization the drug reaches the iris mainly via the circulation of the aqueous.

3 Tonometric readings showed that the intraocular pressure did not rise above 55 mm of mercury (Schiøtz). I realize, therefore, that the magnesium stopped bubbling as soon as it was deprived of its surrounding fluid (aqueous). The result was that the pressure usually settled in the region of 50 to 55 mm of mercury. On one occasion the patient was told to lie face downward, so that the aqueous could still surround the metal implant. Within two hours the intraocular pressure increased from 54 to 76 mm of mercury (Schiøtz). This demonstrated that it was necessary for the patient to lie on his back so that the gas could collect in the anterior chamber and limit the increase of intraocular pressure by depriving the magnesium implant of its surrounding fluid.

The series of bone-free roentgenograms taken on dental film by the method suggested by Vogt² and Clark³ clearly show how the entire anterior chamber is filled with gas, how the gas extends along the metal implant and how it collects under the conjunctiva. It can also be seen that the cyclodialysis tract is being kept open by the gas.

I was able to keep the patient under regular fortnightly observation for five months. The conjunctival congestion disappeared entirely during the three weeks which followed the operation, and the intraocular pressure remained between 24 and 29 mm of mercury (Schiøtz) for almost five months, during which time the lens slowly became opaque and dilated vessels appeared on the iris. At the end of five months after the operation the patient returned, complaining of pain in the eye. The intraocular pressure was increased to 45 mm of mercury. Gonioscopically, a complete circumferential iridocorneal synechia could be seen, and there was no suggestion of the presence of a surgical lesion in the angle. The amount of coarse pigment granules in the dependent part of the angle was in great excess. The eye was removed. Histologic examination of a meridional section of the enucleated eye showed that the tract of the filter had become closed and that a peripheral anterior synechia was present. One could not expect operation for hemorrhagic glaucoma of this type to be successful, but it is noteworthy that the ocular pressure had been kept normal for at least four and a half months by this improved method of cyclodialysis.

² Vogt, A. Skelettfreie Rontgenaufnahme des vorderen Bulbusabschnittes, Schweiz med Wchnschr 53: 982, 1923.

³ Clark, cited by Jackson, E. Radiography of Foreign Bodies in the Eye, Am J Ophth 5:677, 1922.

A South African Negro, aged 38, had chronic non-congestive glaucoma in both eyes. Holt's iridencleisis was performed on the right eye, because gonioscopic evidence shows that in the Negro the trephine hole made in Elliot's operation usually becomes blocked with pigment granules. On the left eye Troncoso's operation for implantation of magnesium was performed, as previously outlined, after gonioscopic examination had shown that the iridocorneal angle was open in the vertical meridian. Although this case was not one of congestive glaucoma, the anterior chamber again became completely filled with gas, as in the preceding case, and a similar series of roentgenograms were obtained. The gas had to be allowed to escape by insertion of a hypodermic needle on four occasions. Tonometric readings were not taken, no tonometer being available at the clinic. The experiment of letting the patient lie with his face downward was again tried, and soon (in two hours) the patient complained of pain in the eye. Digital palpation confirmed the suspicion that the intraocular pressure was very high. After two weeks the eye was again normal in appearance. Examination after eight months showed no decrease in the peripheral visual field, and the intraocular pressure appeared to be normal on digital examination. Gonioscopically, the anterior opening of the cyclodialysis tract could be seen to have remained open. It is to be expected from experience with trephine operations

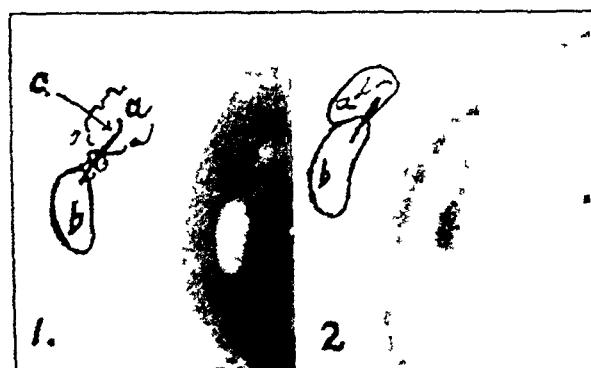


Fig 2—1, roentgenogram taken in Clark's position, showing (a) the subconjunctival bubble of gas, (b) the gas in the anterior chamber and (c) a well marked shadow of the magnesium implant.

2, roentgenogram taken in Clark's position two days later. This shows that the shadow of the magnesium implant (arrow) is more indefinite than that in roentgenogram 1, owing to reduction in the amount of metal by the action of the aqueous.

that excessive deposition of pigment in the eye of the Negro may result soon in blocking the filter again.

I see no reason that Troncoso's method for implantation of magnesium should not be adopted in place of Heine's cyclodialysis. There are indications that by this means a more permanent filter is obtained. I am of the opinion that a single strip of magnesium measuring 5 to 6 by 1 mm is the maximum amount of magnesium to be used, because of the tendency to excessive formation of gas. If this does occur, the gas can be allowed to escape simply by inserting a thin hollow needle through the cornea. Since this operation may be tried by other workers, I thought that it might be of value to record my experience in 2 cases.

Clinical Notes

GONORRHEAL CHOROIDITIS TREATED WITH PENICILLIN

LIEUTENANT HERMAN KRIEGER GOLDBERG (MC), U S N R

Although there have been numerous reports of the efficacy of penicillin in treatment of external ocular conditions, none has indicated that inflammations of the posterior uveal tract are helped. Therefore it is well to report a case of choroiditis in which the result was particularly gratifying.

REPORT OF A CASE

In October 1943 a white man aged 30 was admitted to an overseas base hospital because of arthritis of the spine. While in the ward, he suddenly complained of blurring of vision in the right eye. After consultation with an ophthalmologist a diagnosis of acute choroiditis was made. Foreign protein in the form of triple typhoid vaccine was given, but there was no improvement. Because of the apparent chronicity of the inflammation, he was transferred to the Bainbridge Naval Hospital for further treatment. On his admission to this hospital the eyes were normal externally. Ophthalmoscopic examination of the right eye showed a hazy media, but no details could be seen. A vague outline of a large oval, yellowish area of exudative inflammation could be seen. The margins were indistinct, and the surrounding retina was edematous. This lesion was situated below and temporal but adjacent to the macula. It measured 2 disk diameters. Examination with the slit lamp demonstrated a moderate amount of pigment on the anterior capsule and an occasional precipitate on the posterior surface of the cornea, but there was no aqueous flare. Vision on his admission was 20/400 in the right eye and 20/30 in the left eye and was not improved with glasses.

The patient had been in excellent health except for an attack of gonorrhreal urethritis seven years ago. The condition had been inadequately treated, but the discharge subsided spontaneously.

From Bainbridge Naval Hospital Bainbridge, Md.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

A complete examination of the patient failed to reveal any focus of infection. Examination of the teeth, nose and throat and general medical examinations revealed nothing abnormal. Agglutination tests for Brucella melitensis gave negative results. The white cell count was 10,000, the hemoglobin concentration was 96 per cent, and the urine was normal. The intradermal test with old tuberculin gave a negative reaction to 1 mg. Because of the history of gonorrhea and the presence of a strongly positive reaction to the complement fixation test for the disease and in the absence of any other focus of infection, it was thought that use of penicillin might be indicated. Therefore, the patient was given 160,000 units of the sodium salt of penicillin intramuscularly on each of three successive days. Improvement was noted after twenty-four hours. The media became clearer, and vision was improved to 20/70 at the end of twenty-four hours. Within ten days vision had increased to 20/40. The choroidal lesion lost all ophthalmoscopic evidence of activity. Some pigment was seen to be deposited at the margins of the lesion, the vitreous became completely free of opacities, the edema of the retina subsided, and the details of the fundus could be clearly seen. The choroidal lesion itself seemed to have resolved, and only a minimal amount of scar tissue remained. An additional 300,000 units of penicillin sodium was given two days later, and then its administration was discontinued. Vision has remained 20/40, and there has been no tendency of the inflammation to recur. The maximum improvement occurred within the first ten days.

SUMMARY

Penicillin had been used in 5 other cases of choroiditis, in which the cause was probably tuberculous. There was no improvement, but in this 1 case, in which the etiologic agent seemed to be the gonococcus, the result was spectacular. This response can well be correlated with the specific reaction of other forms of gonococcic infection to penicillin. Penicillin should not be used in the treatment of choroiditis unless the lesion is presumed to be due to gonorrhea.

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Blind

THE ARMY REHABILITATION PROGRAM FOR THE BLINDED AND THE DEAFENED C C HILLMAN, J A M A 125: 321 (June 3) 1944

Hillman recounts the procedure employed for the rehabilitation of the blind. The public idea as to the use of guide dogs is that every blinded person should have one. Experience shows, however, that only about 10 per cent of the blind can use dogs advantageously. Many blinded soldiers will develop the ability to get about with the minimum of assistance. With a skilfully used cane, they are inconspicuous and unencumbered. Some persons do not like dogs, others are temperamentally unfitted for canine companionship. It is important to have determined the type of work to be done and whether a guide dog will be practical and compatible with the future choice of a job. Even when the use of a dog is contemplated, it is better for the blinded person first to develop his complementary senses to the fullest extent. The Veterans Administration and the Medical Department of the Army concur in the belief that a veteran should secure a guide dog only when it is shown that the dog is the best solution of the veteran's problem. Private guide dog agencies have agreed to provide dogs to blinded soldiers, either gratis or at nominal cost. It appears that the facilities of these agencies will be adequate to meet all anticipated needs and that governmental aid in supplying dogs will not be required.

W ZENTMAYER

Color Sense

PERCEPTION OF COLOR SIGNALS BY PERSONS WITH COLOR ANOMALIES UNDER PRACTICING CONDITIONS N WISHNEVSKY and A FLEKKEL, Sovet vestnik oftal 22: 16, 1943

Since from 4 to 10 per cent of young men suffer from congenital disturbance of color sense, the authors consider the possibility of using these persons in aviation. They made tests with color signals in order to find whether candidates with anomalies for color can distinguish colored lights in aviation service, particularly in night flights. The subject was tested with three types of signals (a) colored rockets (red, yellow, green, white) used in aviation, (b) aeronavigation lights and (c) colored signals. A special color signal apparatus was used, and the colored lights were observed on the ground and from the sky, at a

height of from 500 to 1,000 meters. The color sense of the subject was examined with colored plates (Stilling, Ishihara, Robkin) and with Nagel's anomaloscope. The subject registered his findings himself during the night flight, and the records were controlled by the attached physician, whose color sense was normal. Forty-one young subjects were examined. Of these, 29 had deuteranomalyopsia, 7, extreme deuteranomalyopsia, 1, deutanopsia, 1, protanomalyopsia, and 3, protanopsia. Twenty-one were pilots, 12, co-pilots, and 8, radio gunners. The majority had from 50 to 500 flying hours of experience. The authors summarize their study as follows:

Classification of disturbances in color sense according to the Kries-Nagel scheme can be made on the basis of pigment tests and of examination with Nagel's anomaloscope.

Comparison of the data obtained with the pigment tests, the anomaloscope and the color signals and color rockets showed that the majority of mistakes were made by subjects with color blindness and to a lesser degree by the subjects with color anomalousia.

Tests with the yellow and green rockets showed that even the control subjects made mistakes.

The colored signals were incorrectly identified from the ground and from the air by the subjects with color anomalousia, by those with extreme deuteranomalyopsia and by those with other forms of anomalousia, in that order.

The identification of the colored signals during flying is much more difficult than in railroad and automobile transportation because of the small visual angle from which the signal is seen and the short time permitted for distinguishing the signal.

The application of colored signalization in aviation requires the correct differentiation and naming of the color.

O SITCHEVSKA

Congenital Anomalies

THE MARCUS GUNN PHENOMENON REPORT OF A CASE V RAMÍREZ ESTEVA, Arch Asoc para evit ceguera Mexico 1: 163, 1942

The author considers this condition as exceedingly rare, since only about 100 cases have been reported since Marcus Gunn presented his first case before the Ophthalmological Society of the United Kingdom, in 1883.

The author describes the clinical aspects and possible factors in the causation, diagnosis and treatment of the disturbance and reports a case

of the syndrome in a man aged 23. The condition was congenital. Partial ptosis of the upper lid was present, and when the patient opened his mouth there was an involuntary elevation of the right upper lid. A moderate spasm of the right inferior rectus muscle was also present.

W ZENTMAYER

Cornea and Sclera

BLUE SCLERAS, BRITTLE BONES AND DEAFNESS REPORT OF AFFLICTED FAMILY J E FARBER and A E MARGULIS, Arch Int Med 71 658 (May) 1943

Farber and Margulis observed a family of 52 members, 12 of whom presented the syndrome of blue scleras. Seven of these patients have brittle bones, 4 are deaf, and 1 has only blue scleras. Eight are males and 4 females. The condition is transmitted and occurs equally in the two sexes. The physical attributes of small stature, hypermobility of the joints, relaxation of the ligaments and abnormal shape of the head were observed in the afflicted members. Three members of the group were studied in detail. Roentgenograms of the skeleton revealed slender bones, generalized osteoporosis and deformities resulting from multiple fractures.

J A M A (W ZENTMAYER)

CLEARING OF VARIOUS CORNEAL OPACITIES PRELIMINARY REPORT E G LAZAREV, Vestnik oftal 22 7, 1943

The metabolism of the cornea, the cause of leukoma and the role of corneal transplantation in clearing adjacent corneal opacities are discussed in detail. Lazarev made clinical experiments in order to determine the role of excision of the cornea on the clearing of the opacities.

Seven cases of central leukoma of various origins are reported. In 4 cases (5 eyes) a strip of opaque cornea, 2 mm wide and 4 mm long, was excised. In 3 cases the excision of the strip was incomplete, i.e., it remained attached at one end and hung like an apron. In 5 cases vision improved from ability to see hand movements to 0.1, the blood vessels thinned and in some cases they disappeared. In 1 case of recent interstitial keratitis the operation was unsuccessful.

Lazarev thus considers excision of the superficial layers of the opaque cornea (1) as the first stage of penetrating transplantation of the cornea and (2) as a favorable factor in clearing corneal opacities.

O SITCHEVSKA

TREATMENT OF SERPIGINOUS AND OTHER PURULENT ULCERS OF THE CORNEA WITH SODIUM SULFANILAMIDE A GOLDBERG, Vestnik oftal 22-34, 1943

The author used local applications of the soluble sodium salt of sulfanilamide in treatment of

90 patients with keratitis and hypopyon and various other purulent ulcers of the cornea. Sulfanilamide powder was used every three hours the first twenty-four hours and then every three hours during the day until complete epithelialization had occurred (no staining of the cornea with fluorescein). Instillations of a 30 per cent aqueous solution of the drug were then used four to five times a day until all inflammatory symptoms disappeared.

In 81 per cent of patients the ulcer was located in the center of the cornea, and in the majority it was deep and large (from 2.5 to 6 mm). Bacteriologic examinations showed pneumococci in 86 per cent of the eyes. The majority of the patients entered the hospital from six to thirty days after the onset of the disease; nevertheless, the clearing of the ulcers was noticeable on the second or third day after initial treatment. In 66 per cent of patients complete epithelialization of the ulcer was observed in from five to ten days. The hypopyon disappeared in many patients in from one to four days. The final visual acuity of 62 patients was rather high; in 50 patients it was increased from 0.06 to from 0.1 to 0.7.

The results thus obtained in treating purulent corneal ulcers with sodium sulfanilamide are encouraging. The method is a simple and radical one, with no complications. The purulent lesion begins to regress almost immediately, the epithelialization of the ulcer is rapid, and it may be assumed that sulfanilamide activates the regenerative process of the cornea.

O SITCHEVSKA

Experimental Pathology

CONGENITAL MALFORMATIONS OF THE EYES INDUCED IN RATS BY VITAMIN A DEFICIENCY J WARKANY and E SCHRAFFENBERGER Proc Soc Exper Biol & Med 57 49 (Oct) 1944

The authors observed congenital defects of the eyes in the offspring of rats raised on a diet of ground whole wheat, crude casein, brewers' yeast and sodium chloride (diet U) supplemented with very small amounts of carotene and bred on a diet entirely free of carotene and vitamin A (diet W). Diet U made possible slow growth and maturation but no storage of the vitamin. If the growth curves of the rats became flat during this preparatory period, which happened three or four times, each rat was given 5 Gm of horse muscle.

Twenty female rats of a certain strain were raised on diet U until they reached a weight of 150 to 160 Gm and regular estrus cycles were established. Then they were placed on diet W entirely void of vitamin A, and bred to males which had been fed an adequate diet. Within a week the females fed diet W showed pronounced signs of nutritional deficiency, and only 3 mothers carried their litters to or near term.

while 9 females resorbed their embryos. The 3 litters obtained by cesarean section consisted of 19 dead young, all of which had abnormal eyes. In 14 of these young the abnormality could be recognized by external examination. Instead of the closed eyes seen in normal newborn rats "open eyes" of a reddish color were seen. Histologic examination showed that the eyes of all 19 young were abnormal. There was no clear differentiation between lids and cornea and the anterior chamber was present in a rudimentary form only. The vitreous chamber was filled with connective tissue. The retina was folded and disorganized. In several specimens a coloboma of the retina was present.

As controls, 62 females of the same strain were fed diet W supplemented with vitamin A. They had 410 young, none of which showed abnormal open eyes.

P C KRONFILD

General Diseases

TREATMENT OF LEPROUS SCLEROKERATITIS T APARISI, Arch Soc de oftal hispano-am 3. 461 (Nov-Dec) 1943

The most frequent ocular lesion of leprosy is sclerokeratitis. The condition is serious, and in spite of all treatment, it sooner or later ends in destruction of the globe. Besides the routine treatment, Aparisi uses calcium in large doses, as though the lesions were of tuberculous origin. Although calcium does not cure the sclerocorneal process, it checks the progress to some extent and delays the destruction of the anterior segment.

In the routine medical treatment, protein therapy, autohemotherapy, chemotherapy of gold salts and arsenicals, fever therapy (intravenous typhoid vaccine), administration of sodium salicylate by mouth and local application of atropine, ethylmorphine hydrochloride and chaulmoogia oil are employed.

In the incipient form of the disease surgical procedures are used to some advantage. Curettage of the affected zone and coverage with a conjunctival flap have been of benefit.

H F CARRASQUILLO

OCULOGLANDULAR TULAREMIA N A PLETNEVA, Vestnik oftal 22: 11, 1943

In the literature the clinical picture, the diagnosis and the differential diagnosis are reviewed in detail. Professor Pletneva stresses the identity of Parinaud's conjunctivitis and oculoglandular tularemia. The agglutination test is the most important diagnostic means; it gives a positive result in the second week, and the blood contains agglutinins for many months, and even years. The cutaneous allergic test with tularin is the next most important clinical diagnostic method. The disease is transmitted not only by skins of rabbits, rats or squirrels but by dogs, horses and cows and by bites of fleas, mosquitoes and horseflies.

The cases of 4 patients are reported. All were acutely ill, with chills and fever, and the preauricular gland was swollen in all. One patient had a few firm, semitransparent nodules on the conjunctiva, resembling a tuberculous lesion. Biopsy showed only a chronic inflammatory process. For 2 patients the diagnosis was difficult to make, as the lesion (a papule) was in the region of the lacrimal sac and a diagnosis of dacryocystitis was made. 1 of the patients was scheduled for extirpation of the sac, and only when the preauricular, submaxillary and cervical glands became inflamed and an agglutination test was done was the correct diagnosis arrived at.

Therapy is symptomatic, mercury ointment for the ulcers of the skin and convalescent serum are considered of great value in treatment of the oculoglandular form.

O SITCHEVSKA

Glaucoma

ANGIODIATHERMY OF THE LONG POSTERIOR CILIARY ARTERIES AND ITS USE IN THE TREATMENT OF GLAUCOMA D GUERRY, Am J Ophth 27: 1376 (Dec) 1944

Guerry gives the following summary:

"1 The results of coagulating the long posterior ciliary arteries of rabbits, singly and together, are compared with those obtained by Wagenmann after cutting these vessels.

"2 Coagulation of a single long posterior ciliary artery was found to reduce the intraocular pressure in both the rabbit and human for a period of about two weeks. The procedure is relatively harmless.

"3 Coagulation of both long posterior ciliary arteries in the rabbit resulted in phthisis bulbi in 50 per cent of the cases.

"4 The procedure is suggested as a rational substitute for posterior sclerotomy, and as a method of preventing the initial tension rise seen so frequently after cyclodialathermy.

"5 The technique of coagulating by diathermy the nasal long posterior ciliary artery in the human is described."

W S REESE

GLAUCOMA AFTER CATARACT OPERATION B C SHARMA, Indian J Ophth 4: 51 (July) 1943

Sharma states that in a series of 400 cataract extractions in which a conjunctival flap was made not a single instance of glaucoma occurred, whereas in 200 cases in which the incision was made in the cornea without a conjunctival flap 14 instances of glaucoma were noted. He concludes that whenever possible it is advisable to dissect a conjunctival flap in operations for cataract extraction. If glaucoma occurs within a few days after the operation, a paracentesis is done, if this fails, an Elliot trephine operation or a cyclodialysis is performed. The result is often

a failure, especially if the glaucoma is due to the growth of corneal epithelium into the anterior chamber

W ZENTMAYER

Injuries

INTRAOCULAR FOREIGN BODY R OLIVERA LOPEZ Arch Asoc para evit ceguera México 1 • 143, 1942

Olivera Lopez reports a case in which a fragment of stone or steel passed entirely through the cornea, producing a wound with herniation of the iris and diffuse opacities of the lens. A roentgenogram showed the foreign body at the apex of the orbit. One and one-half months later the lens was clear, and examination revealed a black plaque near the posterior pole of the fundus. A panoramic photograph of the fundus established the position of the foreign body, and the fragment was removed by electromagnet through a posterior sclerotomy. The resulting visual acuity was 5/10.

W ZENTMAYER

GUNSHOT WOUNDS OF THE ORBIT A B KATZ NELSON Vestnik oftal 22 13, 1943

At a large hospital at the front orbital injuries constituted about 14 per cent of all injuries of the eye. This proportion, however, increased to about 50 per cent in the hospitals at the rear as a result of the improved diagnostic means, particularly the roentgenoscopic examinations. Since mines and grenades are widely used in this war, injuries of the face and eyes with fragments are much more common than those due to bullets, the ratio being about 77:23. Of the neighboring parts of the face, the nose, and especially the sinuses were injured in 56 per cent of cases. In 25 per cent the fragments were found on the opposite side of the face. Frequently a fragment breaks into a few smaller ones and may injure distant structures.

Isolated injury of the orbital wall was seen in 66 per cent of cases, combined injuries in 34 per cent and injury of both orbits in 11 per cent.

Katznelson bases his classification of gunshot wounds of the orbit on (1) the course and length of the injury canal and (2) the relation of the foreign body to the orbit. The axial penetrating injuries usually cause crushing of the eyeball and its loss. The incidences of injuries of the eyeball in orbital wounds were about as follows: penetrating injuries to the eye with loss of the eyeball, 47 per cent; contusion changes, 35 per cent; neuritis with evulsion of the optic nerve, 6 per cent; ruptures of the choroid and retina, 26 per cent; and no changes in the eye, 9 per cent. Ruptures of the choroid and retina were often the result of contusion injuries. The retinal tears might be multiple. Retinal detachments were rarely observed with simultaneous multiple ruptures of the choroid. The chief observations of Lagrange on contusion changes in the eye were

confirmed in this war, except that choroidal ruptures were observed with tangential injuries of the orbit and that with injuries of the upper orbital wall there were also contusion changes in the eye. There were seen evulsions of the optic nerve, neuritis, optic nerve atrophy and optic neuritis with central scotoma due to injuries of the sphenoid and ethmoid sinuses. A peculiar syndrome—slight exophthalmos, ptosis, complete ophthalmoplegia and trophic degeneration of the cornea—was observed in cases of fracture of the upper orbital fissure, hemorrhage or direct injury of the nerves passing through this fissure.

Treatment concerns only the first aid for and early therapy of gunshot wounds of the orbit. Since gas gangrene develops rarely in the face, primary sutures are indicated in injuries of the lids and conjunctiva. It is essential to preserve all the lid and conjunctival tissue, as it will avert the necessity of plastic operations in the future. All small fragments of bone which have the periosteum and soft tissues partly intact should be preserved, as they will serve for the reconstruction of the orbit later. In cases of severe injuries, with fracture of the walls of the ethmoid and maxillary sinuses, the wound is left open for drainage; accurate débridement should be done. If fragments penetrate the sinuses and there is danger of infection of the meninges, sulfanilamide powder should be used locally and the drug administered internally. In retrobulbar hemorrhages with exophthalmos it is wise to suture the lids in order to prevent ulcerative keratitis. In severe injuries of the orbit it is advisable to do an early enucleation. In large defects of conjunctival tissue no sutures should be applied, as the indication for early prosthesis is much greater. If a discharge is present after enucleation a fistula connecting with one of the sinuses or a foreign body should be looked for.

The article is an extensive and thorough analysis of gunshot wounds of the orbit. A number of case reports give a wealth of information concerning the extensive and varied injuries of the orbit observed in the present war.

O SITCHEVSKA

Lens

JUVENILE CATARACT IN ASSOCIATION WITH DERMATOSIS D M ROLETT, Am J Ophth 27 389 (April) 1944

Rolett reaches the following conclusions with regard to the disease described by Rothmund:

"The important points to be remembered are:

"1 Occurrence of catactous changes in rather young people with typical skin changes which may or may not arise simultaneously."

"2 Evidence of pluiglandular endocrine disturbances"

"3 Skin changes although bearing a similarity are not always of the same origin and are not therefore the cause of the disease."

"4 The development of the cataract is rapid and progressive

"5 The prognosis as to the operation and subsequent vision is favorable

"6 Fortunately the disease is not common

W S REESE

A MODIFICATION OF THE CORNEAL SECTION IN THE OPERATION FOR CATARACT J H BAILEY, Am J Ophth 27: 1253 (Nov) 1944

Bailey gives the following summary

"An operation for cataract is described in which the corneal flap is fashioned by an incision from without inward and perpendicular to the plane of the globe. The advantages of the procedure are enumerated and explained. The instrument employed is a short Bard-Parker handle and an attached blade which is keen, inexpensive, and replaceable." W S REESE

Methods of Examination

A SIMPLE METHOD OF DEMONSTRATING NYSTAGMUS IN CERTAIN MINERS A C REID, Brit J Ophth 28: 598 (Dec) 1944

This note is designed to fill a gap in the diagnosis of a form of nystagmus which it is difficult to demonstrate when the man sits upright in a chair but which results in definite distress at work involving stooping. The miner states that as soon as he straightens up the oscillations cease. Even a rapid approach with the ophthalmoscope cannot catch them. To get around this, the author employs a concave mirror 12 cm in diameter with a curvature of -075 D.

The patient stoops while sitting or kneeling and fixes his gaze on the mirror, when he exclaims that the movements have begun, a beam from a pocket torch is directed on the eye being examined, and the oscillations, magnified, are seen at once in the mirror by the observer.

W ZENTMAYER

Neurology

MYASTHENIA GRAVIS OF OPHTHALMOPLEGIC TYPE J M ZAVALIA, M B ZURBRIGGER and O Russo An argent de oftal 4: 144 (Oct-Dec) 1943

Two cases are reported to stress that myasthenia gravis should be considered in cases of ophthalmoplegia and that there is a simple pharmacologic test to confirm the diagnosis.

The cases presented are those of 2 children, 3 and 8 years old. Both patients presented bilateral external ophthalmoplegia, which was less conspicuous in the morning and became accentuated in the evening. With an injection of

1 cc of prostigmine methylsalicylate the condition of the eyes was brought to almost normal twenty minutes later. The authors consider this test of extreme value in differentiation of congenital ophthalmoplegia and the paralyses of the ocular muscles of any other origin.

They discuss fully the cause, symptoms, diagnosis and treatment of myasthenia gravis.

H F CARRASQUILLO

DIAGNOSIS OR LOCALIZATION OF THE CLAUDE BERNARD-HORNER SYNDROME R R BARRIOS Arch de oftal de Buenos Aires 18: 629 (Nov) 1943

The author states the criteria for localization of the lesion in the sympathetic tract in cases of the Horner syndrome in which no accompanying symptoms make possible such localization.

The lesion producing the condition may be supraganglionic (from the hypothalamus to the anterior horn cells of the cord at the level of the seventh and eighth cervical and the first thoracic vertebrae), preganglionic (from the anterior horn cells to the superior cervical ganglion) and postganglionic (from the superior cervical ganglion to the periphery).

When the lesion is in the first neuron there are signs of sympathetic excitation in the facial or ocular distribution of the nerve. The miosis is not fixed, some activity of the pupil is brought about by sensitive stimuli coming from below the lesion in the tract. There is a higher response to the dilating action of cocaine than in the unaffected eye.

When the lesion is in the second neuron, there is absence of the mydriatic reaction to sensitive stimuli. The mydriatic response to cocaine does not occur as in the case of lesions of the first neuron. The value of the sign of increased pupillary response (mydriasis) to epinephrine, as stated by other observers, is questioned by the author.

When the lesion takes place in the third neuron, the symptoms of sympathetic paralysis are more pronounced. The response to pilocarpine (increased sweating) in the area of distribution of the nerve is greater. This concept, however, is not definite. An increase in the action of epinephrine when the lesion is in the second neuron is questioned by the author. Barrilos has proved experimentally in dogs that acetylcholine produces neuronal excitation (mydriasis and retraction of the nictitating membrane) if the third neuron is intact. The idea is expressed that this test may be made on the human subject. It was found that electric stimulation of the anterior ciliary nerves across the sclera in the anterior segment of the eye produces circumscribed mydriasis if the third neuron is intact.

H F CARRASQUILLO

Ocular Muscles

THE FREQUENCY OF SQUINT M O BOYLE,
Am J Ophth 27: 1413 (Dec) 1944

Boyle's study of the frequency of squint bears out the generally accepted views

The incidence of squint in children is usually between 1 and 2 per cent. In school children convergent squint and in adults divergent squint has the higher incidence. As to the time of onset, 17 per cent of the cases of convergent squint and 22 per cent of the cases of divergent squint develop after the age of 7 years.

W ZENTMAYER

ESSENTIAL REQUIREMENTS FOR A GOOD ORTHOPTIC DEPARTMENT D DICKE, Am J Ophth 27: 1417 (Dec) 1944

Dicke stresses the need of cooperation between the ophthalmologist and the orthoptic technician and the necessity for the latter to understand and be interested in children. She discusses treatment, the necessity for minimal fees and the essential equipment required.

W S REESE

CONGENITAL DEFICIENCY OF ABDUCTION OF THE EYES (DUANE'S SYNDROME) A J ELLIOT,
J Canad M Serv 1: 437, 1944

Elliot reports 3 cases of congenital deficiency in abduction of the eyes. In 1 case a bilateral retraction syndrome was present, while in the other 2 cases a unilateral retraction syndrome was found. A limited review of the literature is given.

The article is illustrated

W ZENTMAYER

' Orbit, Eyeball and Accessory Sinuses

EXOPHTHALMOS SECONDARY TO EDEMA AND DEGENERATIVE CHANGES IN ORBITAL TISSUES M H SOLEY, J Nerv & Ment Dis 99: 865 (May) 1944

Soley discusses the extreme degree of exophthalmos for which Naffziger recommended orbital decompression. At the thyroid clinic of the University of California a considerable number of patients were encountered in whom exophthalmos was a presenting feature, and yet the majority of these patients had about the same degree of hyperthyroidism, the same sized thyroids and the same levels of oxygen consumption as the average run of patients with thyrotoxicosis in whom exophthalmos was not prominent. The author reviews the history of 37 patients with severe exophthalmos. The symptoms of exophthalmos were "pop eyes," excessive watering, photophobia, blurring of vision, either persistent diplopia or diplopia with ocular fatigue, swelling about the eyes, conjunctival injection, scratchy lids, frontal headache and pain on pres-

sure against the eyeball. The signs were exophthalmos, periorbital and scleral edema, injection of the scleras, widened palpebral fissures, lid lag, frequent winking (probably due to drying and irritation of the globe), impaired convergence, often more pronounced in one eye, and, in the worst cases, engorged retinal veins, papilledema and corneal ulceration. Twenty-five of these patients had thyrotoxicosis at the time the exophthalmos was a presenting complaint. Basal metabolic rate, size of the thyroid, age and other factors did not differ materially from those of corresponding routine thyrotoxic patients. Special interest in the problem of exophthalmos probably accounts for the rather large number of patients in whom severe ocular symptoms were noted early in the course of their disease, before they were treated. The author believes it is important to segregate such patients and to consider the condition of their eyes with special care. If the patient has hyperthyroidism when first seen, roentgen therapy to the thyroid is preferred to subtotal thyroidectomy, in order to allow a more gradual return to a healthy thyroid status and to avoid the complication of myxedema. However, if the goiter is large or nodular, operative treatment is still indicated, and the patient should be reexamined frequently afterward. Indications for orbital decompression are changes in function of extraocular muscles (paresis or complete loss of function), impairment of vision, corneal ulceration or pronounced edema of the conjunctivas or scleras. Because progression of exophthalmos occurs in nearly one half of all thyrotoxic patients who have subtotal thyroidectomy for hyperthyroidism, patients in this category should be watched most carefully after thyroidectomy.

J A M A (W ZENTMAYER)

Retina and Optic Nerve

RETRO-BULBAR NEURITIS FIVE CASES DUE TO PARA-NASAL SINUSITIS R FORD, Brit J Ophth 28: 511 (Oct) 1944

Five cases of retrobulbar neuritis supposedly due to paranasal sinusitis are reported. The fact that in the 5 cases vision was recovered after defects lasting as long as two or three, or even twenty-nine years points less to neuritis than to pressure on optic nerve fibers, analogous to that exerted by a pituitary tumor, removal of which even after prolonged pressure on the optic nerve is followed by restored sight. The term "retrobulbar neuritis" is less accurate for the condition than "pressure paresis of the optic nerve." Ford states that it is when the sinusitis is hidden, i.e., when the secretion is retained, that retrobulbar neuritis develops. As soon as it becomes obvious, either spontaneously or through nasal drainage, the retrobulbar neuritis tends to disappear.

W ZENTMAYER

ANGIOMA OF THE RETINA I C MICHAELSON,
Brit J Ophth 28: 522 (Oct) 1944

A sergeant complained of sudden onset of defective vision in the left eye two weeks previously. Visual acuity with a correction of — 6.50 D sph ⊖ 0.50 D cyl, axis 180 was 6/36. Examination of the fundus showed a large retinal detachment, chiefly in the lower quadrant, with a tear in the 4 o'clock meridian about 12 mm from the disk. The inferior temporal artery and vein were broad and tortuous and appeared to end in a raspberry-colored angioma, of about $\frac{1}{3}$ disk diameter. General medical examination revealed nothing abnormal.

Micropuncture was made into the tumor, and three micropunctures were made in a vertical line up and in from the tumor with the intention of catching the feeding artery. Surface diathermy with the micropuncture was used. About three months later visual acuity was 6/9, and the visual field had increased in size. The retina was in position, the tumor appeared occluded, the feeding artery was of normal size, and the draining vein could not be definitely traced.

The article is illustrated

W ZENTMAYER

Trachoma

SULFANILAMIDE IN TREATMENT OF TRACHOMA
L PARADOKSOV, Vestnik oftal 22: 41, 1943

The treatment of trachoma with sulfanilamide has been used since 1940. The dose of sulfanilamide employed was 0.3 cc given five times a day for ten days, the course being repeated three to five times at intervals of five days. Sulfanilamide powder was also applied locally to the conjunctiva of the everted lids once or twice daily. The last therapeutic measure made the patients comfortable. One hundred and fifty patients, most of whom (140) had trachoma 3, were treated; of these, 112 patients had a complication in the form of pannus or, occasionally, ulcer of the cornea, trichiasis or entropion. In some patients, with trachoma 1 and 2, combined expression of the follicles and chemotherapy were employed.

Two tables and the histories of a few patients with persistent trachoma which did not respond to any therapy except administration of sulfanilamide illustrate the effectiveness of chemotherapy.

Paradoksov comes to the following conclusions:

1. Sulfanilamide is an effective remedy in the treatment of trachoma.
2. The combination of expression, or massage, of the follicles and sulfanilamide therapy frequently gave the best results.
3. It is best to have intervals in the course of treatment of trachoma with sulfanilamide.
4. Administration of sulfanilamide, with use of the powder in the conjunctiva, aids greatly in reduc-

tion of the inflammatory process in the cornea (ulcer, pannus) and conjunctiva.

O SITCHEVSKA

Vision

TEMPORARY STIMULATION OF EMMETROPIC VISUAL ACUITY J E. LEBENSOHN and R R SULLIVAN, U S Nav M Bull 43: 1 (July) 1944

Lebensohn and Sullivan say that visuopsychic excitation seems to be the only factor common to the procedures recommended for improving natural vision. An increase of interest, attention and alertness effects keener interpretation of visuosensory stimuli. Drugs that accelerate cortical or sympathetic activity should be effective. This view is supported by recent experiments on one of the fundamental measurements of visual function, the fusion frequency of flicker, which is indicative of the excitability of the visual system. An increase of acuity above that attainable by a careful refraction would emphasize how much the psychic cortex participates in measurements of visual acuity. Fifty men were selected for study whose visual acuity in each eye was 20/20 or better, naturally or with glasses. Acuity was tested on the double broken circles of the Ferree-Rand chart. From a stopwatch record of the ten letter reading, the speed per letter in tenths of a second was noted and the average of three trials recorded. In every subject the eyes were examined separately and binocularly, so that each examination involved three tests for speed and acuity respectively. Each man was tested at 8 a.m. and was then given a placebo as a control or 10 mg of amphetamine sulfate or 3 cc of nikethamide, and the tests were repeated at 10 a.m. and 2 p.m. A consistent improvement in acuity and reading speed was induced by nikethamide and amphetamine in both slow and fast readers. Nikethamide or amphetamine improves reading speed more than visual acuity, but the effect of amphetamine on both visual functions is more pronounced than the effect of nikethamide. Analysis of 150 tests shows that in 44 cases amphetamine was relatively superior to nikethamide in stimulating visual acuity and in 126 cases in increasing reading speed. Amphetamine apparently exerts a more beneficial influence on normal than on ametropic vision. This was proved by comparative tests on 16 persons with ametropia. The authors conclude that the psychogenic origin of many visual complaints is probably insufficiently appreciated. The visuopsychic cortex can be stimulated by various measures, but amphetamine sulfate in small doses (from 5 to 10 mg) is a simple, safe and efficient agent for this purpose.

J A M A (W ZENTMAYER)

Sympathetic Ophthalmia

CHANGES IN THE BLOOD AS A SYMPTOM OF THREATENING SYMPATHETIC OPHTHALMIA
PRELIMINARY REPORT N G RABINOVITCH,
Vestnik oftal 22 20, 1943

The morphologic changes in the blood, particularly the variations in the monocyte count, were observed in 120 cases of severe perforating injury of the eye. In 42 cases the eye was enucleated, and the diagnosis was confirmed by histologic examination; in 78 cases there was severe or mild iridocyclitis. In all but 13 cases in which the eye was enucleated the monocyte count was as high as 8 to 12 per cent. In the second group, of 78 cases, the monocyte count corresponded to the severity of the iridocyclitis, i.e., the count was high with severe iridocyclitis and low with the milder form. In 13 cases in which the eye was enucleated and the histopathologic diagnosis was endophthalmitis the monocyte count was fairly normal. The number of monocytes decreased very slowly after enucleation an indication that the organism was still infected.

Thus, the high monocyte count is a fair indication of threatening sympathetic ophthalmia, and one should be guided by it in deciding to enucleate the injured eye.

O SITCHEVSKA

Therapeutics

ROENTGEN THERAPY OF CERTAIN DISEASES OF THE EYE A BELTIUKOVA, Sovet vestnik oftal 22·35, 1943

Roentgen therapy was used with 51 patients, and the results for 42 of this series were observed

and analyzed fully. In 20 patients with trachoma, secondary glaucoma or iridocyclitis roentgen therapy did not give favorable results. The full history and the course of treatment are given for 22 patients with tuberculosis of the anterior segment of the eye. In all these patients the Mantoux reaction was positive, and the possibility of syphilis was eliminated. Many of the patients had received the usual therapeutic measures for many months or years without results. Nineteen such patients suffered from keratoscleritis (9 had sclerosing keratitis) and inflammation of the iris and ciliary body.

A dose of 160 kilovolts and 4 milliamperes was delivered with a filter of 0.5 mm of copper and 3 mm of aluminum at a distance of 60 cm, usually every twelve days; this dose was from 10 to 20 per cent of the unit skin dose. As a rule, there was an exacerbation of the process for a few days. Frequently a fresh opacity, possibly a leukocyte reaction, was observed in the cornea near the inflammatory lesion. The best results were obtained in the patients with chronic, severe sclerosing keratitis.

Beltiukova summarizes the results as follows:

1. Roentgen therapy gave excellent results in the treatment of keratoscleritis and keratouveitis. The inflammation subsided, there was no recurrence, and vision was improved, so that the patient could resume his industrial work.

2. When a proper dose of from 10 to 20 per cent of the unit skin dose was employed, administered at intervals of twelve days, the general dose being not higher than 60 per cent of the unit skin dose no epilation or cataracts were observed.

O SITCHEVSKA

Society Transactions

EDITED BY DR W L BENEDICT

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

WARREN S REESE, M D, *Chairman*

GEORGE F J KELLY, M D, *Clerk*

Dec 21, 1944

Suprasellar Meningiomas Associated with Scotomatous Field Defects DR N S SCHLEZINGER DR B J ALPERS and DR B P WEISS

In the establishment of a diagnosis of suprasellar tumor such as a meningioma the syndrome of optic nerve atrophy and bitemporal field defects has previously been emphasized. In order further to increase efficiency in establishing an early diagnosis of suprasellar meningioma, we believe that the concept of this syndrome should be broadened to include expanding scotomatous field defects in conjunction with atrophy of the optic disks.

Characteristically, the scotomatous field defects become identifiable as a clue to the existence of a chiasmal lesion by uniting with a peripheral encroachment on the visual field at some point so as to produce an expanding sector defect.

Four cases were described which demonstrate the early occurrence of visual loss with scotomas in the visual fields in patients with suprasellar meningiomas. These cases clearly indicate that the syndrome of such scotomatous field defects and optic nerve atrophy always requires exclusion of the diagnostic possibility of a suprasellar tumor before being attributed to retrobulbar neuritis or multiple sclerosis. Headache is often a prominent feature in cases of suprasellar tumor and aids considerably in directing attention toward such a lesion. In the absence of headache and of deformities of the sella turcica, the combination of optic nerve atrophy and either bitemporal or scotomatous field defects is sufficient to warrant the complete examination of the spinal fluid and pneumoencephalographic study.

REPORT OF CASES

CASE 1—A woman aged 31 was admitted to the hospital on Sept 16 1939 with a history of failing vision for eight months, including a period of partial remission. Examination showed bilateral optic nerve atrophy with a central scotoma of the left eye and a combined central and peripheral field defect of the right eye. There was progression of symptoms with severe headaches for the year prior to her death, on

April 19, 1942, following operation. The diagnosis of suprasellar meningioma was verified.

CASE 2—A girl aged 16 was admitted to the hospital on Jan 18, 1940 with a history of headaches for three years and impairment of vision for four months. Examination showed bilateral optic nerve atrophy with combined central and peripheral field defects of both eyes. Death occurred on Feb 10, 1940, after operation. The diagnosis of suprasellar meningioma was verified.

CASE 3—A woman aged 31 was admitted to the hospital on April 24, 1940 with a history of rapidly failing vision of the right eye for four months and of the left eye for one month. Examination showed anosmia on the left side, bilateral optic nerve atrophy, with papilledema in the right eye, and combined central and peripheral field defects of both eyes. There was progression of visual impairment prior to operation, on May 2, 1940. The patient was discharged, with a verified diagnosis of suprasellar meningioma.

CASE 4—A woman aged 23 was admitted to the hospital on Aug 19, 1942 with a history of headaches and increasing visual impairment of the left eye for three months, followed by failing vision of the right eye for one month. There was optic nerve atrophy in the left eye, with merged central and inferior altitudinal peripheral defects of that eye, and a central scotoma for color in the right eye. Visual impairment was progressive. The diagnosis of suprasellar meningioma was verified.

DISCUSSION

DR WALTER I LILLIE This excellent presentation should not pass without praise. Acute, precipitous visual changes are due to inflammatory, vascular or toxic conditions, while tumors usually produce a slowly progressive visual syndrome. In the prechiasmal area this does not hold true, owing to the anatomic variations, so well described by Shaeffer and de Schweinitz. Suprasellar meningiomas almost always have their origin in the tuberculum sellae (Cushing), and a certain percentage produce a prechiasmal syndrome. The latter group is illustrated by the authors' cases.

One must decide early whether the lesion is inflammatory or neoplastic. A thorough general and neurologic examination, including an examination of the spinal fluid, is important before a definite diagnosis is made. Multiple sclerosis is a common cause of the prechiasmal syndrome, and the spinal fluid usually shows an increase in the number of cells and a colloidal gold curve of zone 1 type. With a chronic type of inflammation—chronic basal arachnoiditis—or with suprasellar tumors metabolic changes occur at the same time as or after the visual disturbances, a point which easily differentiates these lesions from the intrasellar type. The encephalogram is

also an aid in differentiating the suprasellar tumor and chronic basal arachnoiditis

These two conditions are surgical and do not respond to medical therapy. Ophthalmologists should insist on an early diagnosis, so that the neurosurgeon can institute the proper therapy. The results are excellent, the mortality rate is low, and the patient obtains useful vision.

DR N S SCHLEZINGER Dr Lillie has given an excellent discussion of the paper and has emphasized the points which needed stressing.

Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas

DR IRVING H LEOPOLD and (by invitation)
DR WILLIAM O LAMOTTE JR

This paper was published in full in the January 1945 issue of the ARCHIVES, page 43

DISCUSSION

DR FRANCIS HEED ADLER It is not often that the simplest way of treating a disease turns out to be the best, but I believe that these experiments show this to be true in the case of penicillin therapy of acute inflammations of the anterior segment. I have seen sensitivity to penicillin develop in 2 patients when the drug was used locally. I should like to ask Dr Leopold whether he observed sensitization in experimental animals. I should also like to ask whether the organism that he used to obtain experimental keratitis was one which penicillin itself would kill. If so, did he find any difference in the curative value of penicillin with different methods of administration?

DR IRVING H LEOPOLD In answer to Dr Adler's question concerning the development of local sensitivity to the use of penicillin, it is surprising how few cases of sensitization one sees, considering the huge doses of penicillin that have been used systemically, as well as locally. Actually, however, there are reports appearing in the literature which suggest local sensitization to penicillin. Two cases of contact dermatitis due to penicillin have been reported (Binkley, G W, and Brockmole, A. Dermatitis from Penicillin, *Arch Dermat & Syph* 33:326 [Nov] 1944). In the same issue (page 330), Rostenberg refers to a report by Welch and himself that penicillin when injected intradermally will produce sensitivity. Physicians must be on the lookout for allergic manifestations of this drug, as they have been for the sulfonamide compounds. Actually, we have seen no signs of contact dermatitis in the rabbits, but the rabbit is a notoriously poor animal in which to demonstrate such hypersensitivity.

In answer to the second question, this organism, *Pasteurella lepiseptica*, was obtained by routine culture of material from our rabbits' eyes. It is a gram-negative bacillus, which we

found to be sensitive to penicillin. Bacteriologic studies made us think at first that it was a previously undescribed organism, but further study and consultation with Dr L A Julianelle and Dr L F Rettger revealed that the bacillus, although not identical with, most closely resembled *Past. lepiseptica*. We produced corneal infection with this organism in a series of rabbits and compared the therapeutic effectiveness of local and systemic administration of penicillin. The intramuscularly administered penicillin failed to have any influence on the corneal ulcers, whereas all eyes treated locally with penicillin responded well to the therapy.

DR FRANCIS HEED ADLER Then the weight of evidence would point toward local use of the drug in all cases? What evidence there is suggests this method, rather than intramuscular injection.

DR IRVING H LEOPOLD Yes, all studies indicate the superiority of local over systemic administration of penicillin for corneal infections due to penicillin-sensitive organisms.

Syphilitic Iritis, with Particular Reference to the Herxheimer Reaction as a Diagnostic Aid and Response to Different Methods of Treatment, Including Penicillin Therapy

DR JOSEPH V KLAUDER (by invitation) and DR GEORGE J DUBLIN

How valid is the diagnosis of syphilitic iritis when based solely on a positive Wassermann reaction or when made in the late stage of syphilis or in cases in which the duration of infection is unknown? What are the criteria of the efficacy of antisyphilitic treatment in justifying the conclusion that the iritis is due to syphilis? Antisyphilitic treatment exerts a nonspecific effect on iritis. Judgment at times is difficult, since both local treatment and nonspecific therapy exert a favorable action on iritis. The purpose of this paper was to discuss these questions, as well as the Herxheimer reaction of the ocular lesion as evidence of the syphilitic causation. The intensification of the inflammatory process (constituting the Herxheimer reaction) was evaluated by examinations with the slit lamp conducted before and soon after antisyphilitic treatment. The Herxheimer reaction, as observed through the corneal microscope, had not previously been employed in diagnosis.

Of 33 patients with syphilitic iritis, 3 were treated with penicillin. The case record of 1 of these 3 patients was given in detail, the flare-up of the ocular lesion (Herxheimer reaction) after treatment with penicillin was described, and the period required for the iritis to become quiescent and the effect on the lesions of the skin and the mucous membranes were discussed.

In order to avoid too pronounced a Herxheimer reaction and too rapid regression of the

inflammatory lesion (therapeutic paradox), reduced initial doses of penicillin were employed—10,000 units in each of the first four injections, as compared with 50,000 units employed in treatment of early syphilis. A total dose of 2,400,000 units of penicillin was administered to each of 2 patients, and 1,200,000 units of penicillin was administered in treatment of the third patient, who had syphilitic iritis and associated secondary syphilis.

The iritis of the 3 patients treated with penicillin became quiescent within twelve days, as compared with two to five weeks required for patients given chemotherapy or fever treatment combined with chemotherapy.

DISCUSSION

DR ALFRED COWAN I agree with the authors that there are few objective features in syphilitic iritis or uveitis that cannot be found in almost any other type of severe uveitis. In my experience papules are rare. Certainly, ophthalmologists seldom make any distinction between the two forms of iritis, so that to consider some sign as characteristic of syphilitic uveitis is pretty farfetched.

Formerly, a diagnosis of syphilitic iritis was much more readily made than it is today. Then, severe iritis, if the patient was not alcoholic and did not have tuberculosis or rheumatism, was regarded of syphilitic origin. That explains the earlier large proportion of cases of iritis in which syphilis was supposed to be the cause, as compared with the present number of cases of syphilitic iritis.

In how many of the 33 patients did Dr Dublin find lesions resembling papules? I recall that in cases in which the iritis was thought to be syphilitic the ophthalmologist was careful about sending the patient to the syphilitologist before first treating him, lest the treatment should be too severe or by a severe reaction should produce damage that could never be repaired.

DR GEORGE F J KELLY Did these patients show general signs of a Herxheimer reaction, or was this response confined to the eyes? It was stated that the eyes of these patients were examined with the corneal microscope sixteen to eighteen hours after the injection of penicillin. Were they examined before receiving the injections? Dr Dublin referred to penicillin as a spirocheticide. Does he regard that as proved?

DR GEORGE J DUBLIN In reply to Dr Cowan's question whether we saw any nodules in the iris in our series of patients. It is my impression that such lesions were noted in 5 patients. The nodules were distinct masses and were not noted at the first examination. The last patient, who had a large mass in the iris at the time I saw him and described the case to my resident at Wills Hospital, was examined by Dr Cowan three days later.

DR DUBLIN Did Dr Cowan fail to see any nodule? Dr Klaudei referred to this patient as showing tremendous improvement with fever therapy prior to treatment with penicillin. On my first examination, I noted a pronounced massive nodule in the lower portion of the iris below the pupillary border. Five days later there was no evidence of this mass. Slight atrophy of the iris was present at this point. The mass disappeared faster than any that I have ever observed.

In regard to the question whether we noted any general manifestations of too rapid a Herxheimer reaction, it is my belief that such a response occurred only once—in a patient who complained of severe headaches after injection of penicillin. A patient is usually examined with a corneal microscope one or two hours prior to injection of an arsenical and approximately sixteen to eighteen hours after the injection. From 0.30 to 0.45 Gm of neoarsphenamine is given in an attempt to avoid the possibility of too rapid destruction of the tissues or too rapid regression of the lesion.

It is interesting to note the different features of syphilitic iritis with the slit lamp microscope, for this is the first time we have been fortunate enough to be able to see, with a fairly high degree of clearness, pathologic lesions in the anterior segment of the eye. We have divided the Herxheimer reaction into four stages. In the first stage, after eighteen hours, there are some clouding of the cornea, some fine keratitic precipitates and a slight aqueous flare, and in the second stage, pronounced haziness and cloudiness of the cornea, a pronounced aqueous flare with turbidity and many floating cells in the aqueous. In the third stage, all the aforementioned changes are present, together with nodules in the iris. Some of the nodules have a reddish tint, while others are yellowish. All the nodules we have noted have been close to the pupillary border or immediately adjacent to it. In only 1 case was a mass noted near the root of the iris. In the fourth stage there is a spongy exudate (fibrinous iritis) with a "frozen" aqueous.

Prior to the advent of the slit lamp evidence of a Herxheimer reaction was deduced from the appearance of various physical signs, such as headache following injection of an arsenical or rupture of an aneurysm after antisyphilitic treatment. We do not feel that the Herxheimer reaction, particularly as noted with the slit lamp microscope, is an infallible sign of syphilis. We believe, however, that it is of diagnostic aid in a high percentage of cases and is an addition to the evidence obtained by laboratory and clinical methods of examination, including the Wassermann test. Even when there is distinct clinical evidence of syphilis, the Wassermann reaction may be negative. We have had a small percentage of Herxheimer reactions in cases of nonsyphilitic

iritis but we are unable to explain them at this time We are working on a number of control cases, however, and we hope to have more accurate data and to reach more definite conclusions in the near future We do feel, however, that a positive Herxheimer reaction as noted with the slit lamp microscope is an addition to the evidence obtained by laboratory tests

WARREN S REESE, M.D., *Chairman*

GEORGE F J KELLY, M.D., *Clerk*

Jan 18, 1945

Acquired Ptosis Classification and Correction Dr EDMUND B SPAETH

The author presented an analysis of over 200 cases in which acquired ptosis was either the sole complaint or part of the symptom complex of the underlying condition From the data a classification based on anatomic and etiologic characteristics was developed Cases illustrating each division were shown with lantern slides

The varied surgical means for correcting these conditions were presented All forms of symptomatic ptosis are not surgical conditions Those which are need individual attention, depending on the underlying factors

This paper will be published in the *American Journal of Ophthalmology*

DISCUSSION

DR JAMES S SHIPMAN Dr Spaeth has shown many forms of ptosis that many did not know occurred Usually one thinks of ptosis as a congenital condition, which can be corrected by one of many different operations, the reason there are so many operations for ptosis is that none of them is perfect

Dr Spaeth has demonstrated that ptosis does occur after birth, as the result of many factors, and that it is by no means always congenital Before one operates on any patient for ptosis, one should first determine whether or not the condition is congenital If it is a case of acquired ptosis, what is the cause? What is the pathologic condition? Unless these factors are known, one may get into difficulties that could have been avoided Certainly in cases of ptosis due to syphilis or myasthenia gravis, one does not try operative intervention

As Dr Spaeth has shown, the operative principle in correction of acquired ptosis is much the same as that used in correction of the congenital form The cause, the amount of scar tissue and the pathologic process, however, modify a great deal the technic that is to be followed

Aberrations of the Eye DR ALFRED COWAN

Thomas Young, as early as 1801, showed conclusively that the eye is neither achromatic nor aplanatic Many others, particularly Volkmann, Donders, J H Knapp and Tscherning, investigated the aberrations of the eye, but the most thorough study of the actual image of the eye was made by Gullstrand He found that the caustic surface is extremely intricate and that it varies as the meridional section is revolved around the axis

In the eye one has not only all the aberrations which must be eliminated in a well designed artificial optical instrument but the added faults that exist in a living asymmetric organ

The aberrations of the eye are physiologic, and their absence would be of no use to the eye The effect of the circle of least confusion is that of a point image as long as its diameter does not exceed the resolving power of the eye The retina is sensitive to distinct visual acuity only in a very small area at the fovea, and for this reason only that part of the caustic which is found most useful is utilized The surrounding halo is disregarded Also, because of the peculiar structure of the retina, the effects of such factors as marginal astigmatism, curvature of field and distortion are negligible The faults of the optical system of the eye do not interfere with distinct visual acuity

DISCUSSION

DR FRANCIS HEED ADLER This is a valuable paper, and it indicates fair mindedness in at least one physiologic optician The majority seem to have such faith in geometric optics that they are like an economist who wilfully blinds himself to the frailties of human nature in order to believe wholeheartedly in the doctrines of Karl Marx They insist on speaking of point images on the retina, although they know they do not exist This has seriously retarded knowledge of visual physiology, and Dr Lancaster is quite right in emphasizing the importance of learning about image formation in the eye as it occurs in nature, and not as it is pictured in geometric optics I agree with Dr Cowan that geometric optics should be taught as the basis for physiologic optics, but the student must be carried beyond this and instructed in image formation as it actually occurs in the human eye

DR I S TASSMAN I should like to commend Dr Cowan for his excellent presentation and for pointing out the value of retinoscopy in at least obtaining an approximate determination of the refractive state

It seems to me that in recent years there has been a tendency to overemphasize subjective examination in refraction, or at least to emphasize certain subjective tests and methods for determining the result in refraction At the same time, in a great many instances, the objective examina-

tion is neglected A paper of this kind will help to overcome some of the objections that have been raised to objective examination and retinoscopy, particularly in cases in which cycloplegics are employed One of the chief objections to the use of cycloplegics has been the very large pupil and the difficulty in making a retinoscopic examination of the central area

This as Dr Cowan pointed out, should present no difficulty to one with any experience in retinoscopy I should go a step further and add that retinoscopic examinations should be performed in every case preliminary to subjective study regardless of whether or not a cycloplegic has been employed I think it is a mistake that, in the examination of presbyopes especially, retinoscopic examination is often omitted

Infection of the Human Eye with Torula Histolytica DR CHARLES WEISS, DR M C SHEVKY and DR I H PERRY

Through the cooperation of Dr Martin I Green, of San Francisco, we examined material obtained by trephining the sclera of a patient for whom the clinical diagnosis of a possible cyst of the retina had been made The history is briefly as follows

A, a white man aged 56, had been in an automobile accident in 1941 In July 1943 Dr R J Nutting, of Oakland, Calif, discovered a growth in his right eye and enucleated it in October 1943 Three months later the patient complained of poor vision in the left eye He soon manifested mental symptoms and was confined to a sanatorium The eye showed fine deposits on the posterior surface of the cornea and on the anterior surface of the lens There were "floaters" in the aqueous and the vitreous A diagnosis of "possible cyst of the retina with retinal detachment and uveitis" was made The sclera was trephined, and material obtained from culture showed the presence of a yeastlike organism which we identified as *Torula histolytica* (*Cryptococcus hominis*) This is the second case of an ocular infection due to *T histolytica* to be reported in the literature

In its cultural characteristics the organism resembled the torula of Benham and Hopkins' group III when grown in corn meal agar Its ability to ferment carbohydrates was weak and variable No gas was formed Gelatin was not liquefied There was abundant budding, but neither myceliums nor endospores were formed The organism killed mice when injected intraperitoneally or intravenously

When the culture was injected into the anterior chamber of the eyes of rabbits, it was possible to observe early pathologic changes The inferior part of the anterior chamber became opaque, and a pannus developed on the surface of the cornea

Histologically, there was a slight exudate consisting of polymorphonuclear cells and some monocytes along the periphery of the cornea Along the anterior surface of the iris and the posterior surface of the cornea was a delicate festoon of rosettes In the center of each rosette was a torula, surrounded by a single row of cells (polymorphonuclear cells and monocytes) Torulas were seen engulfed in macrophages

DISCUSSION

DR WILLIAM O LAMOTTE JR This organism, known as *T histolytica*, was brought to the attention of my colleagues and myself in the department of ophthalmology of the University Hospital during the past year through an opportunity of observing the eyegrounds of a patient in the orthopedic-pediatric services who subsequently died of an infection with *T histolytica* of such widespread degree that the term torulosis could aptly be applied to it A report of this case will be published soon by Dr Joseph Snyder (Meningitis Due to Infection with *Torula Histolytica* Report of a Case, *Arch Neurol & Psychiat* 53: 392 [May] 1945) resident pathologist at the University Hospital The patient, a 6 year old girl, was originally admitted for treatment of chronic osteomyelitis of the left femur and right humerus with penicillin The offending organism was hemolytic *Staphylococcus aureus* It was not long after her admission that signs of a generalized systemic infection and involvement of the central nervous system appeared, including an increase in the cerebrospinal fluid pressure Many torulas were isolated from the spinal fluid, both on direct smear and by culture Despite massive doses of penicillin, given both intramuscularly and intrathecally, the child died The penicillin therapy did not influence the number of torulas in the spinal fluid It was about six weeks after the first sign of involvement of the central nervous system that the child died During all this time we had the fundus under observation There were no definite changes until a week before her death, at which time bilateral papilledema of 2 to 3 D appeared Also, in the region of the posterior pole of each eye were a number of poorly defined, pale yellow areas, of about $\frac{1}{8}$ disk diameter and deep to the retinal vessels having somewhat the appearance of deep necrosis or thick exudates

At autopsy the orbits were unroofed and the posterior segments of the eyes removed In view of the fact that the torula was found histologically in practically every tissue of the body, it was felt that the presence of torulas might explain the patches observed ophthalmoscopically in the eye before death Sections did show a few nests of the organism in the retina, although not in as great abundance as we expected judging from the lesions seen ophthalmoscopically

I should like to point out that in all the articles that have appeared, and in the recent one by Dr Martin Cohen (*Binocular Papilledema in Case of Torulosis Associated with Hodgkin's Disease*, ARCH OPHTHALMOL 30:477 [Dec] 1944), the statement is made that the genus *Torula* is widespread in nature. I understand from Dr Weidman, however, that an organism which can produce infection both in man and in animals has not been found in nature, that the organisms of this group which are widespread are all saprophytic and that, in his opinion, it is still problematic where the particular organism which causes human infection resides

between the appearance of these relatively infrequently reported cases I was wondering whether in his experiments Dr Weiss used only the organism isolated from his patient or whether he actually attempted to produce animal infection with some of the strains of *Torula* which have been found widespread in nature. Dr Weiss's presentation is instructive, perhaps in the near future, one will be able to make use of diagnostic tests.

DR CHARLES WEISS We used only the strain which we isolated from the patient to produce the lesions in the rabbit's eye.

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

Canadian Ophthalmological Society—The seventh annual meeting will be held in Montreal, Canada, at the Montreal Neurological Institute, 3801 University Street, on Friday, June 15, 1945.

Thursday, June 14—Council meeting and dinner at the University Club of Montreal, 2047 Mansfield Street at 7 p m.

Friday, June 15—Executive Session 9 a m.

Scientific Sessions The following program will be presented 10:30 a m. Dr F A Aylesworth A Study of Causes of Blindness in Over 12,000 Cases in Canada, Dr J A MacMillan The Pathology of Retinal Changes in Tay-Sachs Disease, Dr J E Pelletier Visual Fields with Tangent Screen, Dr A Lloyd Morgan Recession of the Inferior Oblique.

2:30 p m Dr W Gordon M Byers O'Connor Advancement (Cinch) Operation, First Lieutenant Leo S Kirschberg, R C A F (by invitation) Interrelationship of Heterophoria, Stereopsis and Flying Performance in Flying Training, Second Lieutenant J C McCulloch, R C A F (by invitation) Clinical Aspects of Stereopsis, Dr Charles E Davies Orthoptic Treatment in Convergence Insufficiency.

American Orthoptic Council Examinations for Technicians—The next examinations by the American Orthoptic Council will be held in September and October 1945.

The written examinations will be held at various cities in the country on Friday, Septem-

ber 7 Only candidates passing the written examinations will be permitted to take the oral and practical tests, to be given in Chicago, Saturday, October 6.

Applications on official forms must be received before July 1, 1945.

Address The American Orthoptic Council, 23 East Seventy-Ninth Street, New York 21.

American Board of Ophthalmology—An examination will be held by the American Board of Ophthalmology in Los Angeles in January 1946, at the time of the mid-winter course. Applications for this examination must be filed before September 1. Further information may be procured from the secretary, Dr S Judd Beach, Cape Cottage, Maine.

SOCIETY NEWS

Central Illinois Society of Ophthalmology and Otolaryngology—The first meeting of the Central Illinois Society of Ophthalmology and Otolaryngology was held at Bloomington, Ill., April 21 and 22 at the Gailey Eye Clinic. The program consisted of papers on "Normal Action of Extraocular Muscles," "Lesions of the Esophagus," "Relationship of Muscle Imbalances and Refraction, Principles of Ocular Muscle Surgery and Ophthalmic Plastic Procedures" and "Cancer of Larynx and Lateral Sinus Thrombosis."

The officers of the Central Illinois Society will be listed in the "Directory of Ophthalmologic Societies."

Directory of Ophthalmologic Societies*

INTERNATIONAL

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Bailliart, 66 Boulevard Saint-Michel, Paris, 6^e, France

Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ostflandern, Belgium

All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6^e, France

INTERNATIONAL OPHTHALMOLOGIC CONGRESS

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Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President Dr A F MacCallan, 17 Horseferry Rd, London, England

PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President Dr Harry S Gradle, 58 E Washington St, Chicago

Executive Secretaries Dr Conrad Berens, 35 E 70th St, New York Dr M E Alvaro, 1511 Rua Consolação, São Paulo, Brazil

FOREIGN

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Secretary Dr K S Sun

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Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President Dr H T Pi, Peiping Union Medical College, Peiping

Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping

Place Peiping Union Medical College, Peiping Time Last Friday of each month

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Assistant Secretary Dr Stephen de Grósz, University Eye Hospital, Máriaútca 39, Budapest

All correspondence should be addressed to the Assistant Secretary

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Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England

Place Birmingham and Midland Eye Hospital

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

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Secretary Mr William M Muirhead, 70 Upper Hanover St, Sheffield

Place Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation Time October to April

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Secretary Dr D Williams, 193 Macquarie St, Sydney

OPHTHALMOLOGICAL SOCIETY OF EGYPT

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Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo All correspondence should be addressed to the secretary, Dr Mohammed Khalil

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President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India

Secretary Dr H D Dastur, Dadar, Bombay 14, India Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

OXFORD OPHTHALMOLOGICAL CONGRESS

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

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Glasgow, C 3
Secretary Dr Alexander Garrow, 15 Woodside Pl,
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Place Edinburgh and Glasgow, in rotation

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Place Rosario Time Last Saturday of every month,
April to November All correspondence should be addressed to the President

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Secretary Dr R J Masters, 23 E Ohio St, Indian-
apolis
In compliance with the request of the Office of Defense
Transportation and in the interest of the national war
effort a meeting will not be held in 1945

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Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of each month, October to May

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Secretary-Treasurer Dr Lewis Jordon, 1020 S W
Taylor St, Portland
Place Good Samaritan Hospital, Portland Time
Third Tuesday of each month

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Wilkes-Barre
Secretary Pro Tem Dr Paul C Craig, 232 N 5th
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Time Last week in April

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man St, Providence
Secretary-Treasurer Dr Linley C Happ, 124 Water-
man St, Providence
Place Rhode Island Medical Society, Library, Prov-
idence Time 8 30 p m, second Thursday in
October, December, February and April

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Lake City
Secretary-Treasurer Dr Charles Ruggeri Jr, 1120
Boston Bldg, Salt Lake City
Place University Club, Salt Lake City Time 7 00
p m, third Monday of each month

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Time First Monday in January, March, May and
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President Dr B M Cline, 153 Peachtree St N E,
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Acting Secretary Dr A V Hallum, 478 Peachtree
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Place Grady Hospital Time 6 00 p m, fourth Mon-
day of each month, from October to May

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TREATMENT OF BILATERAL RETINOBLASTOMA (RETINAL GLIOMA) SURGICALLY AND BY IRRADIATION

REPORT ON PROGRESS

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AND

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NEW YORK

In 1936 we¹ described the technic of a new method of treatment for bilateral retinoblastoma, with reports on progress up to that date in the cases of 6 patients, all of whom had then been observed for less than five years. The principles of this method of treatment were first, the surgical removal of one eye with the more advanced involvement, and, second, the treatment by fractionated roentgen irradiation of the remaining eye in an attempt to conserve vision. In 1942 we made a second report,² giving the follow-up observations in the previously recorded cases, adding 4 new cases and describing certain modifications in technic.

The purpose of the present communication is to present follow-up data in the cases previously reported and to record the results to date of the treatment in 14 additional cases, which make a total of 24 cases of bilateral retinoblastoma in which treatment was by this method. A short description of the technic will be repeated in this report, and we propose to discuss, further, the clinical course of retinoblastoma following radiation therapy, the relative importance of certain factors of technic and the apparent causes of certain complications of treatment.

From the Head and Neck Service of the Memorial Hospital for the Treatment of Cancer and Allied Diseases

Read before the Section on Ophthalmology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944

1 Martin, H., and Reese, A. B. Treatment of Retinal Gliomas by the Fractionated or Divided Dose Principle of Roentgen Radiation, Arch Ophth 16:733-761 (Nov) 1936

2 Martin, H., and Reese, A. B. Treatment of Retinoblastoma (Retinal Glioma) Surgically and by Irradiation, Arch Ophth 27:40-72 (Jan) 1942

END RESULTS TO DATE IN TWENTY-FOUR CASES OF BILATERAL RETINOBLASTOMA TREATED SURGICALLY AND BY IRRADIATION

In reporting end results in the treatment of cancer, we believe that a five year period of observation is generally accepted as being neces-

TABLE 1.—Five Year End Results in Nine Cases of Bilateral Retinoblastoma Treated Surgically and by Irradiation Prior to July 1939

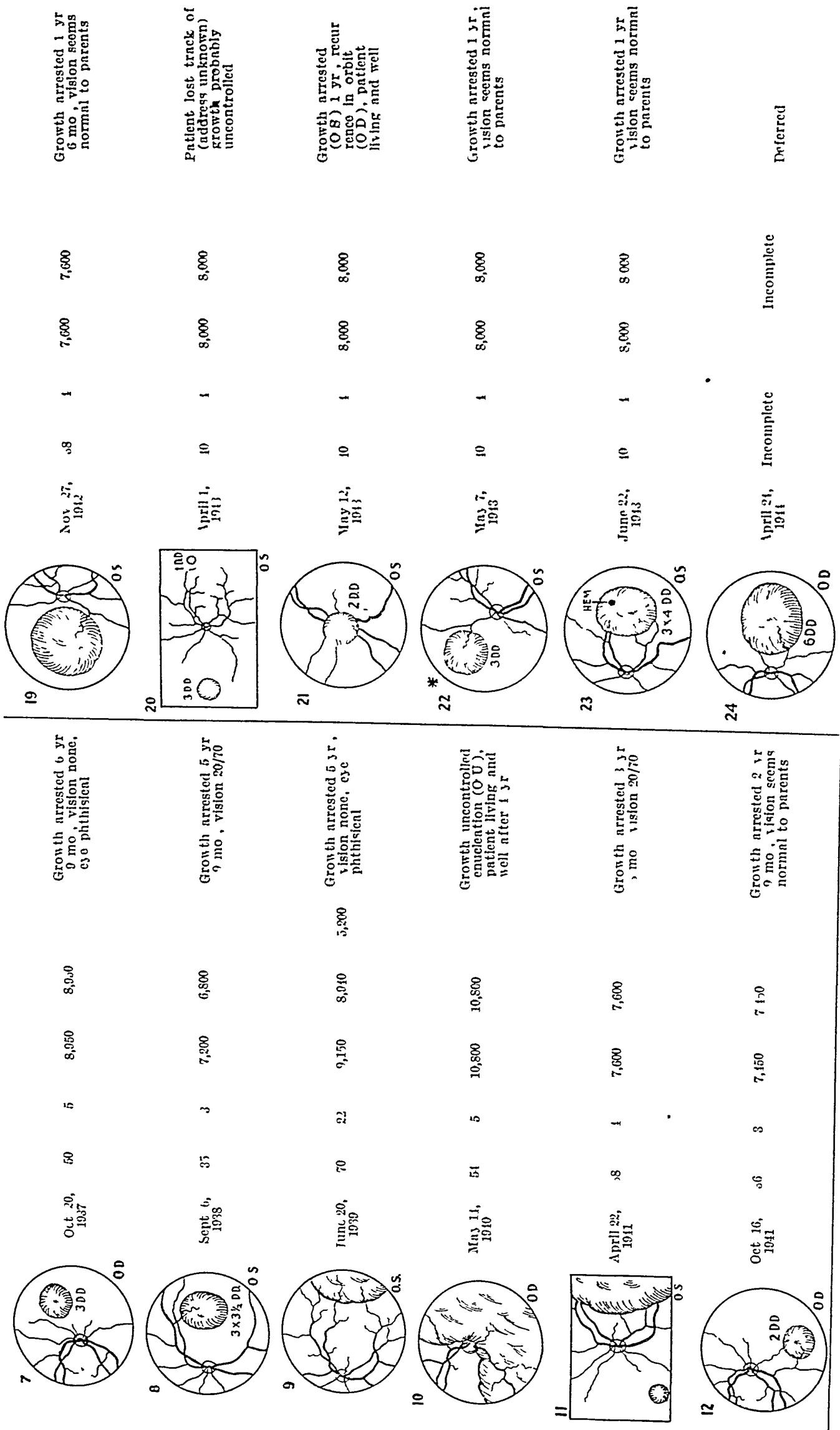
	No. of Cases
Total number of cases	9
Indeterminate outcome	
Death due to cause other than the tumor without recurrence of retinoblastoma	1*
Determinate results	
Total number of cases minus case with indeterminate outcome	8
Failures	
Death due to retinoblastoma	2
Five year end results (calculated on the basis of 8 cases with determinate results)	
Patient living without recurrence and with vision	2 (25%)
Patient living without recurrence but blind	4 (50%)
Total number of patients living without recurrence	6 (75%)

* This patient died of rhabdomyosarcoma arising in temporal muscle 8 years after treatment for retinoblastoma. Patient had good vision in treated eye for over 7 years.

sary before reliable conclusions can be drawn. Our end results in 9 cases of bilateral retinoblastoma in which treatment was given five or more years ago are incorporated in table 1. It will be noted that we have subtracted 1 of these 9 cases in our calculations because the results were indeterminate. In this case, the tumor in the eye regressed completely, and the child had good vision for seven years after treatment but died in the eighth year of rhabdomyosarcoma of the temporal muscle invading the orbit, there being suggestive, but not conclusive,

TABLE 2—Data on Twenty-Four Cases of Bilateral Retinoblastoma Treated Surgically and by Irradiation

Case No. and Location and Size Before Treatment	Date of Admision	Total Treat Period, Mo.			Total Dose in Roentgens		Case No. and Location and Size Before Treatment	Date of Admision	Total Treat Period, Mo.			Total Dose in Roentgens	
		No of treatments	Temporal Portal	Nasal Portal	Fye Direct Portal	No of treatments			No of treatments	Temporal Portal	Nasal Portal	Fye Direct Portal	No of treatments
1	Feb 16, 1933	46	16	10,000	2,400		13	Jan 9, 1932	33	3	6,800	6,400	
2	Sept 29, 1933	73	21	13,000	9,600	1,800	14	Jun 26, 1932	40	5	7,850	7,850	Growth arrested 2 yr 5 mo, vision seems normal to parents
3	Jan 7, 1935	61	15	10,800	10,450	1,750	15	April 8, 1932	38	4	7,600	7,600	Growth arrested 2 yr 4 mo, vision 20/40, slight stationary cataract not in pupillary area
4	March 26, 1935	78	10	11,700	7,500	4,200	16	May 16, 1932	38	4	7,600	7,600	Growth arrested 2 yr 2 mo, vision seems normal to parents
5	May 20, 1935	78	13	11,200	10,800	3,900	17	Aug 10, 1942	40	4	8,000	8,000	Growth uncontrolled patient died
6	Sent 5, 1935	107	14	14,550	14,550	3,250	18	Nov 2, 1942	40	6	8,000	8,000	Growth arrested 1 yr 6 mo, vision none
7							19						Growth arrested 1 yr 6 mo, vision none



* Case 22 is that of a girl aged 2 years and 3 months with bilateral retinoblastoma. The father, now 31 years old, had bilateral retinoblastoma at the age of 13 months. In 1915 both eyes were enucleated by Dr Arnold Knapp, and the case was reported (Arch Ophthalmol 19:575, 1920). The father, totally blind, is a successful lawyer.

evidence that the neoplasm arose as a late result of the irradiation. After necropsy, the microscopic examination of the irradiated eye showed that the retinoblastoma was completely arrested. We felt that the best disposal of this case was to count it neither for nor against the five year cure rate, although we might logically claim a cure.

During the last five years we have employed this method in 14 additional cases of bilateral retinoblastoma. In 3 of these cases the end results are determinate, that is, they are failures since the patients either died of the disease² or have a hopeless recurrence¹. There are also 3 partial failures, although the growth appears to be under control, the patients are blind. Of the last series, of 14 cases, there is freedom from disease with vision in 8 (57 per cent). We present the data on the cases in which treatment was carried out during the last five years as a matter of record rather than of great statistical significance (table 2, cases 11 to 24 inclusive).

Retinoblastoma is a fairly radiosensitive tumor, it can be completely devitalized by a dose of radiation well tolerated by skin, subcutaneous fat, bone, nerve tissue, etc. There would, therefore, be little difficulty in sterilizing such a tumor except for the fact that it is not readily accessible to radiation and lies close to the radiosensitive ciliary body, lens and cornea. A dose of radiation lethal to retinoblastoma invariably destroys vision if it passes through the anterior chamber of the eye. As a matter of fact, the anterior chamber of the eye is so sensitive that it is irreparably injured by even a part of the dose necessary to destroy the tumor. The object of our method of treatment is, therefore, to direct and limit the size of the radiation beam so as to destroy the tumor with conservation of vision.

EARLY RECOGNITION OF RETINOBLASTOMA IN THE SECOND EYE

Retinoblastoma is presumably always a congenital tumor. Regardless of the age at which the tumor is first seen, it was actually present at birth, manifesting itself later because of an increase in size. It is usually stated that retinoblastoma is bilateral in about 25 per cent of cases (unilateral in 75 per cent), but our experience indicates that this figure is much too low and that certainly the growth is bilateral in the majority of instances. In cases of bilateral retinoblastoma, therefore, the tumor in the fellow eye should be demonstrable by careful examination at the time the lesion is recognized in the first eye. The tumor in the first eye is almost never recognized except in an advanced stage, when the growth

has sufficiently filled the vitreous cavity to give a white reflex through the pupillary area and at a time when the tumor in the fellow eye is usually small and in a radiation-curable stage.

The small tumor in the second eye is frequently overlooked at the time the diagnosis is made in the first eye. Of the 24 cases of bilateral retinoblastoma reported by us, the diagnosis of the bilateral character was made in the beginning in only 14. The period of delay before discovery of the tumor in the second eye in the other 10 cases was as follows: twenty-six, twenty-two, nine, eight, six (2 cases), four, three and one (2 cases) month, respectively.

It has been amply demonstrated that the involvement of the two eyes is not due to extension from one to the other but is the result of the multiple origin of the growths. Detection of the lesion in the fellow eye is obviously of the utmost importance since the chances of success in treatment by irradiation are inversely proportionate to the size of the growth.

When the growth in the fellow eye is small and near the equator, or when it is peripheral, it may be easily overlooked. This possibility has impressed us strongly at times during the period of treatment, when we were making monthly examinations of the fundus with the patient under general anesthesia. A lesion observed and charted several times on a diagram as to location and size may not be readily located subsequently even though the examination is made under ideal conditions (general anesthesia, dilation of the pupil and use of a speculum for retraction of the lids and of forceps for rotation of the eye). We feel certain that in every case in which the diagnosis of retinoblastoma has been made in the one eye, the fellow eye should be examined thoroughly under the ideal conditions just stated. The assumption should be that the fellow eye is affected until it is conclusively proved otherwise. Occasionally, retinoblastoma is equally advanced in the two eyes, and then, of course, bilateral enucleation is the only treatment available.

Parents should be taught to know that a white reflex in the pupillary area of a child's eye may be a serious omen and that immediate advice is imperative. In several of our cases such a reflex was ignored for a rather long time. Another sign, occasionally noted first, is a squint, and, for this reason, parents should know that the deviation of an eye of a baby or child may be of more than cosmetic importance. Inequality in the size of the two pupils should also call for prompt advice. There are rare instances in which the parents receive proper advice regarding

the lesion but defer action for an indefinite period, hoping to find some doctor who holds out hope from less radical treatment

SUPPLEMENTARY OBSERVATIONS ON CLINICAL COURSE OF RETINOBLASTOMA FOLLOWING RADIATION THERAPY

In our two preceding reports we described in considerable detail the intraocular changes and the complications following fractionated roentgen radiation therapy in cases of retinoblastoma. This discussion will not be entirely repeated here, but, as a result of systematic reexaminations during and following treatment in the additional cases, we have accumulated much supplementary information on the effects of radiation on retinoblastoma and on the eye in general.

Significance of Size and Form of the Tumor in Prognosis—The smaller the growth, the more favorable is the case for treatment. Generally speaking, the prognosis is not favorable for any lesion occupying more than one quadrant of the fundus. A flat, less elevated retinoblastoma offers a better prognosis than a raised, nodular variety extending forward into the vitreous. Usually, the thickness, or elevation, of the tumor is a greater handicap in treatment than the area covered by the base.

If the tumor reaches the choroid, it grows there with abandon in the rich vascular supply and, in our experience, is uncontrollable by radiation. As soon as this complication is recognized, the eye should be enucleated.

Signs of Regression of the Tumor—Probably the best index of regression is an increase in the calcium content of the tumor, as manifested by chalky white areas, gradually increasing in size and finally coalescing to produce a single, nodular mass of calcium having the appearance of cottage cheese. The increase in the calcium content goes hand in hand with generalized shrinkage of the growth. Around the periphery of the shrunken lesion there may develop a zone of chorioretinitic change in the form of atrophy and proliferation of pigment. In other cases portions of the tumor may disappear, and some small growths may vanish completely, leaving little trace.

Complications—The several complications which occur in the treatment of retinoblastoma were fully described in our previous reports.

Glaucoma occurs mainly either because of over-irradiation of the posterior portion of the eye, beyond the safe limit, or because even a small portion of the otherwise safe dose has passed through the anterior chamber of the eye. These

factors are discussed in detail under subsequent headings.

Among our cases in which irradiation was successful we have had only 2 instances of cataract. In 1 case it was necessary to remove the lens, and in the other the changes were slight, non-progressive and outside the pupillary area, with little interference with vision. These cataracts occurred in the first 2 patients whom we treated before we devised our present special apparatus and before we fully appreciated the need for accuracy in directing the beam of roentgen rays.

In our cases in which the treatment was not successful, with the growth uncontrolled despite irradiation beyond the safe limit, and in which the eye proceeded to atrophy and phthisis, there was, of course, no opportunity to rule out the development of cataract. As a matter of fact, with such advanced pathologic changes, cataract occurs irrespective of irradiation.

Late Vascular Changes—In some of our earlier cases we observed peculiar changes in the fundus six to eighteen months after treatment was started, and at that time we believed that the tumors had not been controlled by radiation and that the growths were progressing. These changes consisted of hemorrhages over and around the site of the lesion, or at distal sites, particularly around the optic disk, with opacity of the adjacent part of the retina. At first we interpreted these findings, especially the hemorrhages, as signs of regrowth of the tumor. These interpretations led us to give additional radiation after an interval of several months of apparent control. In almost all instances in which additional radiation was given for these reasons, the function of the eye was lost as a result of new complications, namely, iridocyclitis, keratitis, intractable glaucoma and, ultimately, atrophy of the globe. As we became more experienced with the upper limit of tolerance of the eye to irradiation, we made it a rule not to go beyond the "safe point" no matter what the indication for further treatment, either at the end of the first course of treatment or subsequently. Since our last report we have been agreeably surprised to find that by rigid limitation of the dose of radiation, as hereinafter described, in many of the cases with late hemorrhages and opacities the condition has followed an entirely benign course, with neither recurrence nor further disturbance in function. We now recognize such changes as being vascular in character, consistent with alterations occurring in other heavily irradiated tissues.

Undoubtedly several factors enter into the explanation of these late vascular changes. The irradiation obviously causes atresia of the vessels,

and secondary vascularity appears from the surrounding, less affected vessels. These newly formed vessels, which grow into the site of the irradiated lesion, are thin walled and tortuous, resembling the vessels in irradiated skin and there called telangiectases. A possible factor in their formation is the atresia of a portion of the normal, smaller veins and capillaries as a result of the irradiation, with consequent dilatation of the vessels which remain so as to provide for a collateral circulation. Telangiectatic blood vessels are always more fragile than normal vessels, and in the retina such vessels are probably easily ruptured when the local blood pressure rises with increased pressure in the jugular venous area, where the veins have no valves. The jugular venous pressure, as well as the pressure in the intracranial and intraorbital regions, together with the pressure in the thorax, is raised with coughing, sneezing and vomiting.

Acute occlusion of arteries and veins may also be a late occurrence, the thrombosed veins giving rise to immediate hemorrhage and transudate over the region drained. The cloudiness and opacity of the lesion and of the adjacent retina are undoubtedly due to ischemia, edema or transudate, the factor involved depending on the type of vascular lesion.

We have noted that in any irradiated eye there may develop in the macular region around the fovea residual edema or multiple white deposits similar to the lesions commonly seen in nephritis, diabetes and the late stages of essential hypertension and known as the "star of the macula." Such macular lesions in irradiated eyes are secondary to late vascular changes. Two instances of this lesion have been noted in our series. In 1 case, in which the tumor was observed clinically and later examined microscopically, the macular deposits had an appearance and a staining reaction similar to macular lesions seen in the other diseases just mentioned.

TECHNIC OF FRACTIONATED RADIATION THERAPY OF RETINOBLASTOMA

In our second report² we described the apparatus, the irradiation factors and the technic of application of the radiation. These data are briefly summarized later in the present report, and the method is illustrated in figures 1, 2, 3 and 4. For a more detailed description of the technic the reader is referred to our previous publications. While we concede that results comparable to ours may possibly be obtained by a somewhat different set of treatment factors, nevertheless we question the wisdom of the introduction of any modification before a thorough

trial has been given the technic which we have found to be successful in a fair percentage of cases. When a physician first attempts to employ a new (to him) method of treatment, there is always a hazard to the patient in disregarding, or changing, tested and recommended treatment factors. Some of these factors are, of course, arbitrary and optional, but others are of paramount importance. For the beginner, it is sometimes impossible to tell which are significant.

Since our first report was published, eight years ago, we have been disappointed to find in the literature the record of only a single case of retinoblastoma treated with fractionated radiation, the results in which are as yet indeterminate (after two and a half years). This case was reported by Tice and Curran,³ who used a "modification" of our technic. Just what the modification was is not stated. We know of

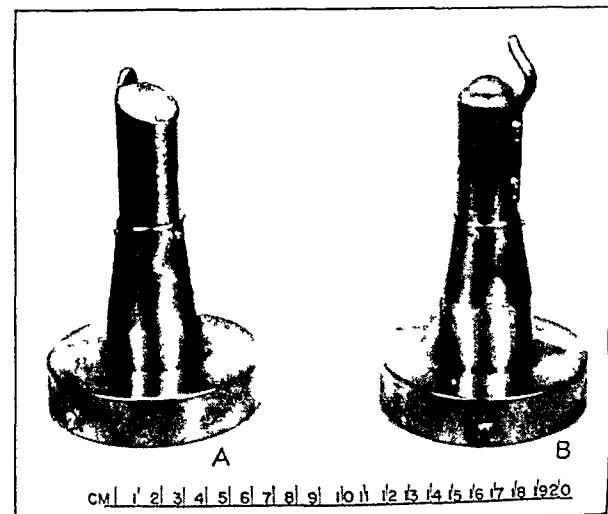


Fig 1.—Special cylinders for radiation treatment of retinoblastoma. *A* has an oblique distal end to fit against the temple. *B* is applied to the bridge of the nose to irradiate a growth in the retina on the contralateral side. It has a hooked projection to mark the margin of the beam of radiation, so that the cornea and the anterior chamber of the eye may be spared.

several other instances in which attempts were made to use our method, in all of which, so far as we know, the results were failures, we suspect because of injudicious modifications in the factors of treatment. Even at the risk of seeming dogmatic, we recommend that before any change is made the technic we have described be followed as closely as conditions permit until the therapist has become thoroughly familiar with it and with its results.

Some of the treatment factors outlined in our second report were somewhat modified from

³ Tice, G. M., and Curran, E. J. Treatment of Retinoblastoma. Radiation Therapy Supplementing Surgical Treatment, Radiology 42:20-33 (Jan.) 1944.

the factors we recommended in our first, for the reason that we discovered several causes of previous failures. We have not subsequently found any reason to modify our technic from that described in our second report, except to limit definitely the total dose and not to give supplementary radiation for apparent recurrences. Some of the general aspects of the treat-

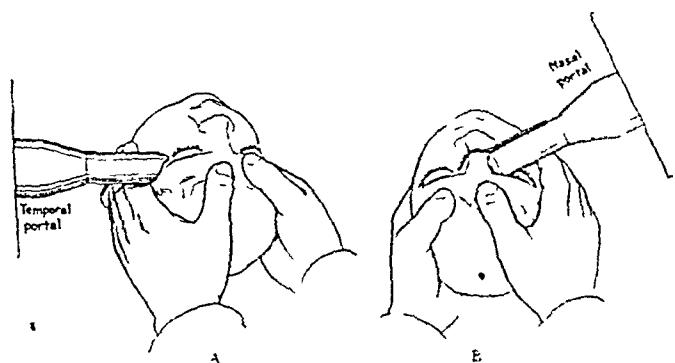


Fig 2.—Roentgen irradiation of retinoblastoma (A) The child's head is being held in position for irradiation of the posterior half of the left globe through a temporal portal (B) The child's head is being held in position for irradiation of the posterior wall of the left globe through an oblique portal from the opposite side of the bridge of the nose

ment require special emphasis, and these will be discussed under separate headings.

Immobilization of the Child During Treatment—The holding of a crying, struggling

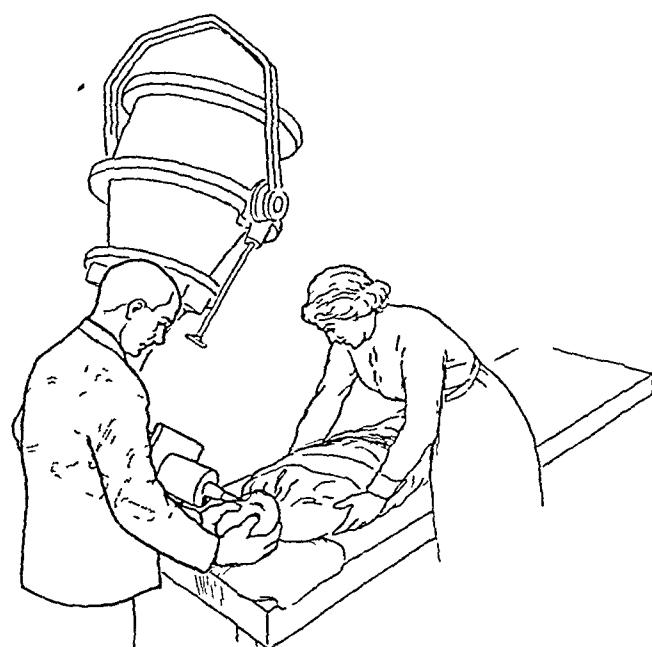


Fig 3.—The child's body is immobilized by being wrapped in a sheet. One of the parents steadies the child's body, and the other holds the head in position during the treatment.

baby under an x-ray machine (fig 3) for about ten minutes three times a week over a period of several months is an onerous undertaking. Such a task should, obviously, be the duty of the parents, or of other members of the family

who, though invariably willing, sometimes find it difficult, unfortunately, to understand what is required and how to follow directions. It is the responsibility of the therapist, nevertheless, to see that the parents comprehend what they are to do and that they realize the importance of maintaining the head in an exact position, so that the beam will pass precisely through the posterior half of the globe and not through the anterior chamber (fig 2). A great deal of patience is often required to teach the less intelligent and less dexterous parents, and until they acquire facility and confidence it may be prudent to give two or three mock treatments. Despite such difficulties, we advise that the therapist make no compromise, such as increasing the diameter of the portal to lessen the requirements for accurate direction of the beam. We feel that it is neither humane nor safe to immobilize the child by purely mechanical means.

Apparatus—Originally we used no special apparatus, except a metal cylinder of 25 cm in diameter with which we had some success

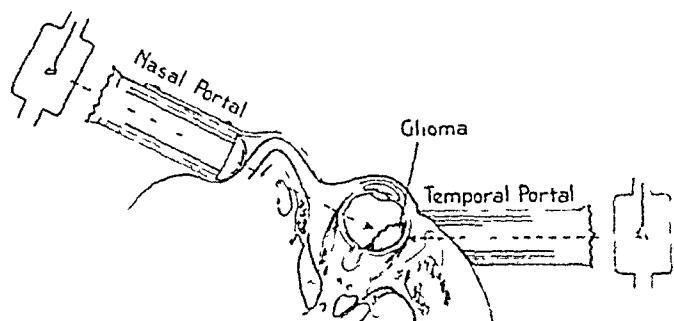


Fig 4.—Local anatomy of the tumor. Cross section diagram showing the path and the objective of the roentgen radiation as directed through each of two portals.

In other cases, however, serious complications, sufficient to determine the difference between success and failure, resulted from the use of this rather crude apparatus. Since we devised the special cylinders illustrated in figure 1, the task of holding the child has become simpler, and inaccuracy in directing the beam and most of the danger of damaging irradiation of the sensitive anterior chamber have been avoided. We feel, therefore, that such special apparatus greatly increases the chance of success and should be used rather than any makeshift device.

Shape, Size and Position of the Skin Portal—The size of the skin portal is undoubtedly one of the most important factors. The limit of accuracy in the direction of the beam of roentgen rays in these cases can hardly go further than to make certain that the radiation passes directly through the posterior half of the globe, in which the tumor always lies. Since the dose of radia-

tion lethal to retinoblastoma approaches the tolerance of the normal structures of the posterior half of the eye and exceeds the tolerance of the structures of the anterior chamber (lens, ciliary body, etc.), the size of the portal should be reduced to its smallest practical diameter and the beam so directed that no radiation strikes the anterior chamber. In our opinion, the practical size of such a portal is about 2.5 cm in diameter, and probably there is no better shape than circular. A portal 3 cm in diameter is, we believe, unnecessarily large and if centered over the retinal tumor will either include the anterior chamber or permit unnecessary irradiation of the orbital tissue posterior to the globe. Some of the unsuccessful results of which we have knowledge were, we believe, due to injudicious modifications of our technic, for example, the use of a larger portal, 3.5 to 4 cm, supposedly to relieve the therapist of the necessity of accurate centering. All of these attempts, so far as we know, resulted in failure.

As we described in our preceding article,² only two portals should be used, namely, a temporal and a nasal oblique (fig 4). For a time we also used a portal centered directly over the pupil of the eye and directed backward. Even though we limited the dose through this portal to from 2,000 to 3,000 r, serious complications in the eye invariably developed, resulting in blindness eventually.

The treatment factors now used by us for retinoblastoma are as follows:

Voltage	250 k v
Target-skin distance	60 cm
Filter	1.5 mm copper (equivalent)
Portal size (circular)	2.5 cm in diameter
Position of portals (figs 2-4)	
(1) Temporal—directed transversely	
(2) Nasal—directed obliquely	
Frequency of treatments	3 times a week
Single dose	400 r
Maximum total dose	8,000 r X 2

In our earlier cases we used roentgen radiation at 200 kilovolts and 0.5 mm copper filter, with which the maximum and optimum dose proved to be about 7,000 r to each of the two portals. We have found, however, that with the factors now being used (250 kilovolts, 1.5 mm copper filter, etc.) the maximum and optimum limit of useful dosage is about 8,000 r to each of these two portals.⁴ With the latter set

⁴ We have found that, all other factors being equal, the dose as expressed in roentgens should be increased by about 10 per cent if translated from that given at 200 kilovolts with a 0.5 mm copper filter to that required for the same clinical effect at 250 kilovolts with a 1.5 mm copper filter. This rule will of course also apply in reverse.

of factors, we have not obtained successful results with doses of less than 7,400 r X 2 or of over 8,000 r X 2. As already stated, we have also learned by bitter experience that should the tumor not regress after a dose of about 8,000 r X 2 (250 kilovolts, etc.) or should it show evidence of regrowth after several months, further irradiation not only is useless but invariably will bring on glaucoma, ending in blindness. We suspect that had we avoided supplemental irradiation (after the initial dosage of about 7,000 r X 2 at 200 kilovolts) in some of our first 9 cases, in which treatment was given prior to July 1939, our cure rate with vision would have exceeded the reported 25 per cent. If after a total dose of 8,000 r X 2 has been given with the aforementioned factors there is definite clinical evidence of residual growth, the eye should be enucleated. We have already described certain findings in the irradiated eye simulating regrowth of the tumor which in most cases we believe are benign in character and not a cause for alarm.

Justifiable Variations in Treatment Factors.—In 1933 we began the treatment of retinoblastoma by fractionated roentgen radiation at 200 kilovolts with a filter of 0.5 mm copper, principally because high voltage apparatus of that particular form was then the standard at Memorial Hospital. A target-skin distance of 60 cm was selected arbitrarily, chiefly for the reason that it was easier to immobilize and hold the child at this, rather than at a lesser, distance from the tube. At present we are using roentgen radiation at 250 kilovolts with a 1.5 mm copper filter because this is now the standard form high voltage x-ray apparatus at the Memorial Hospital. We are of the opinion, however, that results comparable to ours can be obtained with any of the commonly used higher roentgen voltages (180 to 400 kilovolts) and with any filter of 0.5 mm copper (equivalent) or upward. The target-skin distance should be at least 50 cm, but with the use of our special cylinders it will be more convenient to use 60 cm.

The frequency, or spacing, of the individual treatments (three times a week) and the size of the individual dose (400 r) have been selected by us to permit giving an uninterrupted series of treatments at the maximum rate of dosage increment short of causing unduly severe cutaneous reactions. With a more rapid rate of dosage increment the cutaneous reactions become troublesome. It is possible that, with these same factors, treatments of 600 r could be given twice a week with results comparable to those secured from 400 r three times a week, the main

disadvantage of the former being that both parents and child might object to the longer individual periods of treatment.

The most important factors regarding treatment, that is, those factors which will permit of the least variation from our recommended technic, are, we believe, the size of the treatment portal of 25 cm., the use of the special apparatus previously described and the accurate direction of the beam so that irradiation of the anterior chamber is avoided.

Reexamination of Child Under General Anesthesia—If one could be certain that there is now no more to be learned from the systematic reexamination of patients with retinoblastoma while receiving this form of treatment, one might conclude from the foregoing discussion that, since we recommend a somewhat standardized technic and total dosage, frequent reexaminations would be unnecessary. On the other hand, it is only by such reexaminations, under the most favorable conditions, that one can determine the progress and the untoward complications in individual cases and learn to treat, or to avoid, complications incident to radiation therapy of retinoblastoma.

Since the beginning of this work, in 1933, it has been our practice to reexamine the patients at monthly intervals and under general anesthesia while they were undergoing treatment and for the first six or eight months afterward. After about a year the patients are examined at longer intervals (two or three months), and as the children grow older the examinations in some cases, but not in all, can be made without anesthesia. Some of our patients have had systematic examinations in this manner for a period of several years, receiving a total of twenty-five to thirty anesthesias. Such a program consists of more than a mere statement of the facts.

If such a routine should be interpreted as requiring the formal admission of the child to the hospital once a month and the administration of ether by the usual methods, it is probable that the program would be found too arduous and troublesome to carry out as a monthly procedure for any great length of time. We have found evidence of this difficulty in the cases of follow-up observation by ophthalmologists after the removal of one eye supposedly for unilateral retinoblastoma. The ophthalmologist, finding it too trying to arrange for ether anesthesia, has contented himself with infrequent examinations of the remaining eye without anesthesias. In several such instances the tumor in the second eye became far advanced and in the end was discovered by the parents, who finally observed the tumor through the pupil.

We believe that we have found a reasonably satisfactory solution of the difficulty. Up to this time, we ourselves have carried out all the ophthalmoscopic examinations on our patients. One of us (H. M.) administers the anesthetic and the other (A. B. R.) makes the ophthalmoscopic examination. With the facilities available to us, these examinations can be most expeditiously carried out for both clinic and private patients in one of our private offices. We have anesthetized and examined as many as ten children in the space of one hour and had them all out and on their way home within an hour and a half of the start of our project. The children are brought to the office early in the morning by special appointment, the patients having received instructions to omit breakfast and to instill homatropine at least one hour before arriving at the office. Chloroform is used as the anesthetic.⁵ The induction takes only one or two minutes. The ophthalmoscopic examination then begins immediately and continues as long as the child lies still, usually two or three minutes. If a longer time is required, the mask is replaced for a minute or two, until

⁵ Our procedure for giving a short chloroform anesthesia is as follows. The body of the child is immobilized by being wrapped in a sheet. The administration of anesthesia is not begun until the ophthalmoscopist stands at the side of the examining table with his instruments ready to begin his examination, without any loss of time. A standard anesthetic mask, with six or eight thicknesses of gauze, is saturated with 3 to 5 cc of chloroform, and the chloroform bottle is recorked and set aside. Chloroform is never dripped onto the mask, either during the induction or to maintain anesthesia. The mask is placed over the child's nose and mouth without any towel to impede free access of air. At the beginning the child will, of course, struggle and cry, then as anesthesia begins, the breathing becomes irregular and noisy, and within one or two minutes the breathing becomes regular and rhythmic. As soon as the regular and rhythmic respiration is noted, anesthesia is deep enough to permit the manipulations necessary for ophthalmoscopic examination. Without any loss of time the mask is then removed, the lights are turned out and the ophthalmoscopic examination proceeds as long as the child lies quietly, which is usually about two or three minutes. In the darkness, the anesthetist must depend on his sense of hearing to make certain that respiration continues. Attention should be given to holding the jaw forward, so that there will be no obstruction to respiration. The examination continues until the child begins to struggle, then if more time is required, the mask is rewet with chloroform (the bottle recorked and set aside) and again applied until the breathing becomes regular. There can be no question but that chloroform is a safe and uniquely valuable substance for induction of short anesthesia for a child if given in this manner. The precaution of not dripping the chloroform from the bottle onto the mask precludes overdosage. The omission of a towel about the mask insures an adequate oxygen intake.

the child quiets down Afterward the partly conscious child is carried into the rest room, he is completely awake in about ten minutes and leaves the office under his own power in about thirty minutes more There is rarely any nausea In 150 or more examinations over a period of the last eleven years no untoward complication has occurred with the anesthesia, or after it, which appeared to be alarming in the slightest degree, and no parent has objected to the repetition of the procedure, no examination has been deferred or omitted, because of any difficulty concerned with the anesthesia To one who has given short chloroform anesthesia for ophthalmoscopic examinations to children by this routine, the contrast to the tedious admission to a hospital, the ether anesthesia and the long, and sometimes distressing, recovery is obvious

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ABSTRACT OF DISCUSSION

DR A F M DEROETTH, Spokane, Wash
The outcome of this disease without treatment is blindness, followed by a miserable death An investigation by Netherland ophthalmologists placed the incidence of retinoblastoma as 1 case in 34 000 births, a ratio indicating that 12 to 20 cases of bilateral retinoblastoma occur each year in the United States

In 50 per cent of the 24 cases in which the authors employed their method of treatment the tumor was arrested or a cure was effected, with resulting preservation of vision This percentage can be improved if the condition is discovered at an early stage The authors call attention to early signs which may indicate retinoblastoma Their introduction of the use of a general anesthetic for the thorough examination of these small children is to be welcomed

It was my good fortune to refer a patient to the author three years ago Although the tumor is located in the macula, vision is now 20/70 Calcification of the tumor is still progressing, and the area of choroidal atrophy around the necrotic mass is enlarging The child has another small tumor in the periphery, which has a typical "cottage cheese" appearance, an excellent characterization of the mass of calcified foci

Retinoblastoma is radioresistant, and a large dose of radiation is necessary to destroy the growth As to other treatment for this condition, a few permanent cures have been effected with radium radon seeds and perforating diathermy, as in the cases of Schonberg, Moore and Stallard In Budapest, in 1938, my associates and I treated bilateral retinoblastoma with perforating diathermy in 2 cases This method was first employed by Weve In 1 case the tumor was progressive after four or five months, but in the other case the growth was arrested and the pa-

tient was apparently cured one year after the operation Would it be advisable to treat a small tumor with perforating diathermy combined with fractional irradiation?

I should like to stress the responsibility of the physician for the offspring of these cured patients He should impress the parents of the patient, and later the patient himself, with the possibility of the hereditary character of the tumor

This procedure in the hands of the authors saves life and vision in half the cases of this deadly disease

DR RICHARD C GAMBLE, Chicago The authors have correctly termed their paper a report of progress, which indeed it is It is interesting to read their earlier papers, published in 1936 and 1942, and then to read this article One finds some change in technic, but little change in their interpretation of the effects of radiation on the tumor and on the normal ocular tissues, as shown by careful study of the fundus One finds considerable confirmation of the value of the procedure Dr Reese's observations on the changes in the fundus are classic, they should be carefully studied by any physician who has under his observation a patient with such a condition, for they state clearly when enough radiation has been given

I have treated a few patients with bilateral retinoblastoma, and I have always used radium instead of roentgen radiation I do not yet have the special cylinders that the authors have devised to limit the rays to a small portal, so I have felt that it was better to use radon seeds than to expose the entire eye to roentgen radiation with almost certain damage to the lens, cornea and conjunctiva if a sufficient dose is given

With the use of radon seeds the frequent small doses cannot be given However, the effect of radon seeds can be supplemented by use of radium applicators over the temporal portal as often as necessary The employment of such applicators fastened to a bridge in front of the pupil has had bad results In 1 case it seemed to cause a severe pannus, which nullified an otherwise excellent result It is interesting to see that the authors gave some radiation through the pupil in their earlier cases but discontinued the use of this portal after having discouraging results, in the form of phthisical eyes, blindness and death This point deserves emphasis because attention to the danger involved in the future will save many patients from needless suffering and blindness

The results obtained by Dr Martin and Dr Reese are magnificent To arrest the growth in 12 of 24 cases with preservation of vision and to save the eyeball without vision in 5 other cases is an achievement

With regard to the cases in which the growth invades the choroid, the authors apparently feel

that the fractionated radiation method is useless. It is too slow. I should like to ask their opinion with regard to the possible value of treating this type of tumor by means of a Weve diathermy trocar plunged directly into the main mass and by making several rings of micro-punctures around this to seal off the choroid, much as is done to close the hole in a case of retinal detachment.

DR ALGERNON B REESE, New York: Dr de Roeth's suggestion with regard to the supplementation of radiation with diathermy sounds feasible to me, particularly in view of the favorable effects that diathermy had in the cases he cited. It adds an extra hazard, how-

ever, and I wonder whether the advantages outweigh the possible disadvantages. I prefer not to use diathermy for the time being, until it can definitely be proved whether or not radiation alone is adequate.

I agree with Dr Gamble that it would be much better to apply radon seeds than to use diffuse roentgen radiation. In cases in which the tumor has reached the choroid, it is my feeling that no treatment is of value, since the tumor grows so rapidly in the vascular bed of the choroid that any measure directed toward control of the growth leads to destruction of the eye. I believe that therefore in such cases enucleation is indicated.

OCULAR WAR NEUROSES

CAPTAIN HENRY L BIRGE*
MEDICAL CORPS, ARMY OF THE UNITED STATES

The importance of psychologic tension in producing syndromes resembling organic disease first received widespread recognition during World War I. We were left with the now outmoded terms of "soldier's heart" and "shell shock." Since that time the importance of the psychologic aspect of medicine has increased until it borders on the strategic. The present war has already gone through phases known as the "war of nerves."

This paper has a twofold purpose (1) the closer integration of psychiatric states presenting ocular symptoms with the specialty of ophthalmology and (2) the analysis of a series of cases of diseases of the eyes with special reference to psychiatry.

One of the difficulties of treating psychiatry and ophthalmology in one paper is that the terminology and the classification of psychiatric disease are not yet as uniform as are their counterparts in the older specialty of ophthalmology. To the variations in psychiatric terminology must be added the variations in the neuroses and psychoses at different stages of evacuation from combat areas and in various theaters and zones of war. Another confusing factor in the evaluation of psychiatric problems is that many patients, especially those with mild disorders, are never examined by a psychiatrist. The increasing importance of the psychiatric side of medicine places more responsibility for proper psychiatric diagnosis on specialists in other branches of the medical profession. It is as serious for a patient with an ocular complaint to have a physician who neglects the psychiatric side of his case as it is for him to have one who neglects the ophthalmologic or other medical aspects.

MATERIAL AND METHODS

The material for the present study was taken from records of a series of 2,500 refractions and ophthalmic examinations made by the same staff, under my direction, in the eye clinic at the Station Hospital, Stockton Field, Calif.

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All patients were subject to the same approach, that is, they were examined because of their ocular complaints. A complete ophthalmic survey was performed including recording of the patient's history, examination of the external eye, the status of the ocular muscles and the visual fields, study of the ocular fundus, and, in most cases, refraction under cycloplegia.

The diagnosis of ocular neurosis was made by exclusion, at the end of the examination. The theory adhered to was that most persons had a reason for their complaints, and only when no organic cause was found was a condition labeled neurosis.

In ophthalmology there are several variables to be considered before a diagnosis of neurosis can be made. One of them is the low limit of refractive error that may give rise to ocular pain. Unfortunately, many physicians think of hysterical blindness as the most important type of ocular neurosis. On occasion dramatic instances of this occur, such as that of the student pilot who went blind on his first solo flight and had to land his plane by following directions given over the radio by an officer in the control tower. But the majority of cases of ocular neuroses are of a less dramatic variety. They are so similar in history and complaint to cases of true pathologic conditions of the eye that they cannot be differentiated without an ophthalmic examination. The experience of my colleagues and myself has shown that many ophthalmologists do not properly evaluate the type and degree of the neurotic symptoms in conjunction with the ocular findings. Conversely, other diagnosticians may attribute all the ocular pains to neurosis when ophthalmic examination will reveal an organic cause for the pain in the eyes.

Records of patients with ocular complaints were surveyed from the psychiatric point of view. It was found that there were three groups of persons with ocular symptoms (1) persons with simple psychoneuroses, (2) persons with psychosomatic conditions, with the relative importance of the neurotic and the organic disturbance different in each case, and (3) persons with strictly organic disorders.

The incidence of neurotic patients in the group studied was low as compared with the proportion of neurotic patients (80 per cent, if the general impression is correct) encountered in unspecialized civilian practice.

Most of the patients studied were members of the ground personnel of the Army Air Forces, and little ocular neurosis was found in flying personnel except that coincident with serious visual disease. Malingering was a rarity.

A large majority of the patients studied had a refractive error, a muscular anomaly or some other condition requiring either medical or surgical treatment; these patients were considered free of neurosis. A small minority of the patients studied had a history of neurosis but were found to have an organic basis for many of these symptoms; these patients were considered to have psychomatic ocular disease. Except for a chart of the visual fields in case 1, figures, charts and diagrams have been omitted from this study because of previously mentioned variables beyond immediate control.

OCULAR WAR NEUROSES

In general the war neuroses form a clinical entity based on anxiety. They are similar to the traumatic neuroses seen in civilian practice. They may occur in either the acute or the chronic form, and frequently one patient will go through various stages of a neurosis. They present a wide variety of syndromes,¹ with most of which this paper is not primarily concerned.

Ocular neuroses form a small and unimportant group of war neuroses. They are of importance, however, to the ophthalmologist, who is called on to recognize them and to see that they get the proper treatment. In an attempt to give a true picture of ocular neuroses in their relation both to psychiatry and to ophthalmology and to set them in their proper light among other war neuroses, it is necessary to outline a loose classification of the various types of neurosis.

I Psychoses

A Organic

- 1 With infectious diseases
- 2 With disturbances of circulation and exhaustion
- 3 Senile and involutional
- 4 With metabolic diseases
- 5 With new growths

B Toxic

- 1 Caused by alcohol
- 2 Caused by gases, metals, drugs, etc

C Traumatic

- 1 Traumatic delirium
- 2 Post-traumatic personality disorders
- 3 Post-traumatic mental deterioration

D Functional

- 1 Manic-depressive psychosis
- 2 Dementia praecox
- 3 Paranoia
- 4 With psychopathic personality
- 5 With mental deficiency
- 6 Undiagnosed forms

II Psychoneuroses

A Anxiety states

- 1 Acute psychoses
 - (a) Severe
 - (b) Mild
- 2 Chronic psychoneuroses
 - (a) Early stress
 - (b) Established tension
 - (c) Exhaustion

B Hysteria, conversion type

C Psychasthenia or compulsive states

D Neurasthenia and hypochondriasis

E Reactive depression

III Psychosomatic states

IV Malingering

Considering the variable diagnostic criteria of psychiatrists and the variable syndromes in each neurotic state as it is affected by the relative

¹ Grinker, R. R., and Spiegel, J. P. *War Neuroses in North Africa*, New York, Josiah Macy, Jr. Foundation, 1943. Miller, E. *The Neuroses in War*, New York, The Macmillan Company, 1943.

proximity of the patient to the battle front or to bombing attacks, it becomes more important than ever to emphasize the group to which a patient belongs rather than to use terms of more limited diagnostic coverage.

Causes of War Neuroses, Including Ocular Neuroses—The war neuroses of all types, especially the anxiety states, are not so dependent on abnormal psychiatric backgrounds as are the civilian neuroses. War neuroses are predominantly due to present stress and strain. The present study is not concerned with the acute, severe forms of war neurosis that bring soldiers back from the battlefields in psychotic states, the result of constant noise and turmoil, the killing and the danger of war. The anxiety from these causes, the mental conflict between duty and the instinct of self preservation, the fatigue and privation are obvious causes of their condition.

Ocular anxiety neuroses are of mild type, in contrast to severe anxiety states, which result from battle experience, resemble a true psychosis and are often diagnosed as schizophrenia. The ocular neurosis, like the gastric or the cardiac neurosis, is seen behind the lines. It is of the chronic type and is similar in many respects to that seen in civilian practice. The conflict is often, for instance, one of frustration, due in part to lack of promotion after long service and in part to other long-sustained states of dissatisfaction associated with Army life. Frequently there are several conflicts, each of which contributes its share to the vicious circle of dissatisfaction, insomnia and fatigue. It is rarely a single disappointment that brings on the anxiety state. Usually it is the cumulative effect of the relentless conflict, whatever it (or they) may be, with no hope of relief, that sets the neurosis in motion. The mental conflict leads to anxiety, and anxiety leads to excitement of the emergency mechanism and to overaction of the autonomic nervous system. An anxiety state comes into being in the stage of early stress.² It may either progress to the stage of established tension or subside. The anxiety state becomes pathologic when it persists in the absence of stimuli sufficient to cause normal anxiety.

Physical factors, like hunger, thirst and exposure, also have considerable bearing on the acute neuroses of the front lines. In the zones of the interior these factors are usually absent, as are shelling and blast injuries. Fatigue is a factor frequently associated with development of the neurotic states. Not always is the fatigue that of

² Stephenson, G. V., and Cameron, K. *Anxiety States in the Navy*, Brit M J 2 603-607 (Nov 13) 1943.

physical exhaustion. It may be the type that comes from performing a dull task over a long period.

Some neurotic persons undoubtedly have an inherited tendency to anxiety. In others there is no evidence of either hereditary tendency or previous episodes of anxiety.

Sexual conflicts do not seem to have much bearing on the anxiety type of war neurosis. They may constitute one factor underlying chronic maladjustment, but other factors outweigh this aspect in most cases. It is not necessary to go into the relation of the hypothalamus, the cortex and the autonomic nervous system in this paper.

Some Common Types of War Neuroses—The term constitutional inadequacy covers a loosely classified group that includes various neurotic states, as well as some psychosomatic conditions, but it implies some deficiency in the inheritance of the patient and usually exists apart from the anxiety states.

Hysteria is often confused with the anxiety state. Hysterical states develop from conflicts between the cortical centers which are the seat of the sense of duty and the lower centers of the brain, whose chief function is one of self preservation. These states occur most frequently in suggestible persons. An uncritical personality is often associated with hysterical manifestations.

The obsessive states are more complicated and may show up in cases of long-standing anxiety, especially in introspective personalities.

Syndrome of Ocular Anxiety Neurosis—Anxiety states vary as to type and degree. One person may be seen in different stages of the anxiety state at different times. The anxiety syndrome of the advanced clearing station is the anxiety state in its most severe form. The anxiety states seen in men behind the lines are milder and are often not disabling, although they undoubtedly would progress to the severe type rapidly if the person affected were subjected to the mental trauma of battle. Morale and the presence or absence of treatment, as well as the man's tolerance for anxiety, make the breaking point of each person different.

No attempt is made here to separate the syndrome of the ocular anxiety neurosis into subgroups according to type or degree. It is helpful in understanding how the anxiety state develops to think of the stages of "early stress," "established tension" and "anxiety with exhaustion," but for the form involving the eyes this subclassification is unnecessary.

Ocular neurosis is not often associated with complaints referable to other organs, although

when other organs are involved, whether organically or functionally, the neurosis is less likely to be cured and is apt to come to a focus in some site other than the eye.

The ocular neurosis is not usually a disabling state. It is often associated with insomnia. Headache is one of the most frequent symptoms, although the neurosis may simulate almost any type of ocular disease. It has, however, never simulated glaucoma in my experience.³ This is an important point, because in some textbooks the syndrome of ocular neurosis is described as involving blurred vision and the seeing of halos around lights, symptoms which, together with ocular pain and headache, are suggestive of chronic simple glaucoma to the ophthalmologist. In the anxiety state headaches, ocular pains and easy visual fatigue are common. Often there is twitching of the lids, which may develop into true blepharospasm. When blepharospasm develops it becomes a form of hysteria. While anxiety in a mild form is susceptible to wilful control by relaxation, when the patients are seen the tics of the eyelids and the blepharospasm have gone beyond the point where they are controllable. Photophobia is a frequent finding, and many patients with ocular anxiety neurosis cannot be comfortable without colored glasses.

The headaches cause serious interference with efficiency. Often they are of daily occurrence, and they may persist for weeks, being poorly relieved, if at all, by 12 or more acetylsalicylic acid tablets a day. The headaches may be found in patients who report having had cranial trauma in childhood without sufficient damage to justify the disturbance being classified as a post-traumatic syndrome. The headaches frequently appear to be atypical migraine, although they usually do not respond to ergotamine tartrate. The headaches were described by 2 patients as different from migraine headache, which these patients also had. These headaches are sometimes associated with subjective disturbances in depth perception, although the tests for depth perception give normal results. The disturbances in perspective are difficult for the patient to describe. There is often a complaint of dizziness.

The visual disturbances associated with anxiety neuroses vary from transient attacks of blurred vision to transient spells of complete blindness, in which a patient will have to pull his car off the road for ten or more minutes. We have examined several such patients shortly after their attacks.

³ Weiss, E., and English, O. S. *Psychosomatic Medicine*, Philadelphia, W. B. Saunders Company, 1943, pp. 35 and 490.

and have always found the eyes and the visual acuity normal and the visual fields normal in all respects

Under the tension of the physical examination for overseas service, we noted several patients with anxiety states who showed a loss of 40 to 50 per cent in visual acuity and whose vision returned to normal during the relative calm of a subsequent examination of the eyes. None of these patients required tests for malingering. The same apparatus was used for the two tests. During the lengthy ophthalmic examination, the numerous tests of muscular function and of the visual fields and the interval of waiting for the cycloplegic, the patients became relaxed, and their vision returned to normal. Only 1 of this group exhibited transient hypertension as a reaction to the sphygmomanometric determination, and he also showed generalized narrowing of his retinal arteries, grade II, without sclerosis or retinopathy.

Contrary to another contention of the textbooks, the visual fields in this series of patients with ocular neuroses were normal more often than not. The well known gun barrel type of field was found frequently in patients with severe ocular neuroses, especially in men of low intelligence. It is more apt, however, to be associated with hysterical or obsessive states than with simple chronic anxiety. Ring scotoma was often found and was probably associated with the easy fatigability of these patients. Interlacing of the color fields is also pathognomonic of a functional ocular disorder. This finding is comparatively rare, in our experience, and many diagnoses are made without it on the basis of other functional disturbances.

Patients with ocular neuroses of the anxiety type frequently complain of seeing spots or webs in front of their eyes. These spots move with movements of the eyes and are always more vividly seen on a light background. The functional variety of spots before the eyes is termed *muscae volitantes* and is usually associated with normal corrected visual acuity. In the absence of precipitates on the lens or the cornea, of opacities in the vitreous or of chorioretinitis, these spots are entirely harmless, and yet they cause endless trouble to the patient, as well as to the examining physicians, from the gastroenterologist and the neurologist back to the ophthalmologist.

One of the discomforts of the ocular neurosis is the burning of the eyes that is associated with epiphora. Watering of the eyes is transient, is worse in cold weather and is not related to obstruction of the tear ducts or to abnormal secretion of tears, although the lacrimal glands may be

affected by the overfunctioning of the autonomic nervous system in anxiety states.

The syndrome of the ocular anxiety state may be said to include the following complaints with sufficient regularity to make it apparent almost immediately on talking with the patient: ocular pain, headache, twitching eyelids, spots before the eyes and burning of the eyes, with epiphora, photophobia and occasional distortion of perspective. Other evidence of neurosis is often apparent, such as insomnia, perspiration of the palms, occasionally a speech defect and often a history of nervousness.

CASE 1—A private aged 20 suddenly went blind at roll call. He had already had one attack of blindness the week before. In each instance the blindness was of short duration. The patient stated that he had had severe headaches steadily for two weeks previous to this admission to the hospital.

Ophthalmic examination was made after physical examination and revealed nothing abnormal. Vision of 20/200 was improved to 20/15 with the following correction: right eye, —1.50 D sph; —1.25 D cyl., axis 180; left eye, —1.50 D sph; —1.00 D cyl.

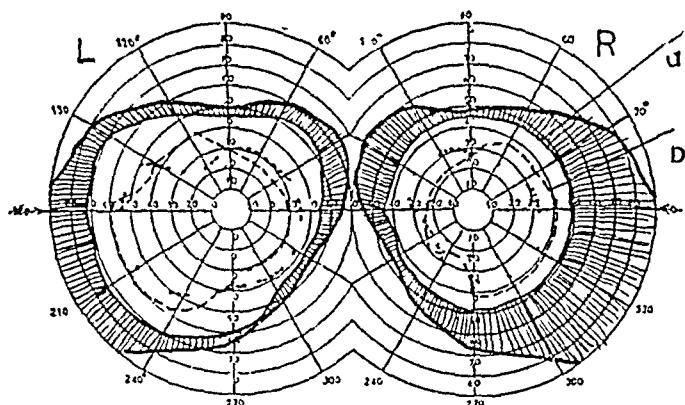


Chart of interlacing color fields. The field for 3/330 white (a) is essentially normal. The field for 5/330 red (b) interlaces in each eye with field for 5/330 blue (line of dots).

axis 180. Orthophoria was present. The visual fields showed moderate interlacing of color fields. The form field was normal. The blindspots were normal (right 5 by 6 mm and left 6 by 6 mm) with white. The external and the internal eye were normal.

The patient's glasses were not changed, he returned to duty and carried on successfully.

CASE 2—A private aged 24 complained of blurred vision accompanied with severe headaches, which he had had for several weeks. His eyes felt tired at the end of a day's work. He had twitching of the eyelids, which had been increasing during the past few days.

His history included overseas service in China and the Philippines, but he did not attribute his nervousness to war experience. He had noted nervousness since the age of 12 years, when he was unconscious for fifty-two hours after a severe fall. During his youth he had fainted several times from excitement. He had had several attacks of abdominal pain during the past year, and on one occasion he was admitted to an Army hospital because of the possibility of appendicitis. The diagnosis at discharge was psychoneurosis. He had had enuresis until the age of 16 years.

Examination revealed a person whose voice quavered with emotion and who perspired freely at a comfortable

room temperature Refraction under a cycloplegic gave the following results In the right eye, with a +0.25 D sph \perp +0.50 D cyl, axis 85 vision was 20/15, in the left eye, with a +0.25 D sph \perp +0.50 D cyl, axis 90, it was 20/15 The external eye was normal There was exophoria of 1 prism diopter and no hyperphoria Convergence was 7 prism diopters Divergence power was 3 prism diopters The visual fields and the fundi were normal No glasses were prescribed

This patient received a short furlough and returned to duty He was able to understand his nervous makeup and planned to take steps to prevent nervous exhaustion

CASE 3—A private aged 24 complained that he had broken his glasses and could not get along without them He stated that he got headaches and inflamed eyes from not wearing them

Ophthalmic examination revealed that the eyes were entirely normal both externally and internally The muscular balance was normal There was 1 prism diopter of exophoria and no hyperphoria Convergence was 22 prism diopters Divergence was 12 prism diopters The visual fields were entirely normal Cycloplegic refraction revealed vision of 20/15 in each eye with the following correction right, +0.50 D sph \perp +0.50 D cyl, axis 100, left, +0.50 D sph \perp +0.75 D cyl, axis 75 The patient had been wearing (and had vision of 20/20 with) glasses with the following corrections right eye, +0.25 D sph, left eye, +0.25 D sph This represented to us a false idea on the part of the patient, namely, that he needed glasses for constant wear We found no other evidence of neurosis and tried to convince the patient that he would get along as well without glasses

It might be argued that this patient needed his full cylindric correction We have often prescribed cylinders of this strength This case is cited to emphasize the importance of weighing the psychoneurotic symptoms against the ocular findings We felt that since the patient had been happy with a simple sphere, there was no need to correct his cylinder, and that most of his trouble was psychologic

These 3 cases illustrate the fact that ocular neurosis has no relation to refractive error In some cases orthometropia is associated with weighty symptoms On the other hand, large refractive errors are found in truly neurotic persons

CASE 4—A guard aged 22 was referred to the eye clinic because of his ocular complaints and a question of compensation

His chief complaint was that he saw a spot before one eye that looked like a cluster of small bubbles He also had headaches and stated that his eyes frequently became red He attributed all his symptoms to an injury sustained when a shingle blew off a roof and struck him in the right eye while he was patrolling The accident happened in April 1942 He was treated for two days in the dispensary, and when the bandage over the eye was removed he saw the spot in front of his right eye He was sent to the clinic because the spot had enlarged to such an extent that it could now blot out a jeep 50 feet (15 meters) away Immediately after the injury he had been referred to a civilian eye, ear, nose and throat specialist who treated the eye for a while and then discharged him as cured Because

of his continual complaints the patient was referred to an Army hospital, where he saw another eye, ear, nose and throat specialist This physician saw a small opacity in the lens, which he mentioned to the patient Examination of this spot in my clinic showed it to be congenital and no larger than a speck of dust

At a later date the patient was referred to San Francisco, where an ophthalmologist who examined him stated that there was evidence of an old hemorrhage in the retina We did not see the patient until fifteen months after the injury, but at that time there were no scars in the retina

Examination revealed that the patient had blepharospasm Vision was 20/100 uncorrected in the right eye and 20/30 in the left Externally both eyes showed moderate redness, due to mild follicular conjunctivitis Local use of eye drops was prescribed

Considerable time was required for examination of the patient because of his apprehension, but finally a careful observation of the fundus was made The only ocular abnormality was the previously mentioned congenital opacity of the lens, the size of a speck of dust The cornea and the media were clear There was no evidence of a retinal detachment The choroid showed normal pigmentation in the periphery The nerve head was distinct and without pallor

Visual fields were taken with some difficulty because of the pain which the patient felt in his eye during the examination The fields showed a generalized contraction in the right eye but were normal in the left eye Refraction under a cycloplegic showed that vision of 20/20 could be obtained in the right eye with +0.50 D sph and in the left eye with +0.25 D sph \perp +0.25 D cyl, axis 99 Measurement of the phorias was normal

The spot seen by the patient was visible only on a light background and was not visible ophthalmoscopically, nor did it show as a scotoma on examination of the visual fields It was diagnosed as *muscae volitantes*

Had this patient's complaints been recognized as psychoneurotic by the first four physicians who saw him, he never would have progressed to the acute state of ocular anxiety neurosis

The psychic element in every case should be determined before treatment or other disposition is made In cases of injury or suspected disease of a highly specialized organ such as the eye, specialized consultation is advisable Only the physician who is absolutely sure of himself can diagnose the absence of organic disease In cases of doubt a neurosis grows luxuriantly

Differential Diagnosis—It is not yet entirely clear just where the dividing line lies between the refractive errors that do and those that do not cause ocular pain and asthenopia Undoubtedly many persons who have a smaller error than 1.25 D need glasses Especially in cylindric corrections does one see symptoms relieved by 0.50 and 0.75 D In myopia a spherical correction of 0.50 D makes a great difference and often relieves asthenopia which is unaccompanied with neurosis The dividing line between neurotic and pathologic is not definite It must be drawn in each case by estimating the weight of each factor

The cases which are considered to involve neuroses in this series are those in which the patients did not have sufficient pathologic changes in the eyes to justify their complaints. That must be the basis of the diagnosis in every case. It leaves a variable factor—the physician—which will become more nearly a constant as more attention is paid to the neuroses. Another variable is the degree of nervous exhaustion in the patient, especially in the patient with an anxiety state. In wartime this is almost always greater than in peacetime. In patients with nervous exhaustion a small defect may give rise to disabling psychosomatic symptoms, or the exhaustion may be a factor in a simple neurosis.

Hysteria and the Obsessive State.—Hysterical and obsessive phenomena in patients with ocular neuroses seem to have more relation to the genetic background and to a previous neurosis, especially one of a long standing, than do anxiety neuroses with ocular manifestations. These conditions are too complicated for the ophthalmologist to classify psychiatrically.

Some of these manifestations are defense mechanisms. Most of them are not associated with anxiety, although they may be found in untreated or poorly treated anxiety states of long duration. In the majority of patients with these conditions there is bland complacency. Hysterical and obsessive states were rarely encountered in this series. The following cases illustrate the obsessive state, or conversion hysteria.

CASE 5.—A private aged 21 reported for an ophthalmic examination because his head "felt light." He had noted this feeling all his life, but it became worse after he entered the Army. He had no ocular complaints, although he had insomnia. He was able to do all his work without difficulty. He sat quietly without looking at the examiner and showed evidence of being introverted and of the schizoid type. He was not interested in reading; when pressed, he admitted that he liked to bowl but said he had not done much of it in the Army.

Examination revealed his vision to be 20/80 in the right eye and 20/100 in the left. He was able to read 0.75 M with each eye. The refractive error was as follows: right eye, +0.25 D sph ∕ +0.50 D cyl, axis 105 (vision 20/80); left eye, +0.50 D sph ∕ +0.50 D cyl, axis 15 (vision 20/100).

The visual field was contracted to within 30 degrees in each eye, and a relative central scotoma was present in each eye. The blindspots could not be mapped out because of lack of cooperation. There were 4 prism diopters of esophoria, 18 prism diopters of convergence and 12 prism diopters of divergence. External examination gave normal results; ophthalmoscopic examination revealed only a remnant of a pupillary membrane in the right eye. Examination showed the fundus to be normal.

Vision of 20/80 and 20/100 is too poor to enable a person to do all the things this patient did without difficulty. He was not alarmed by the poor vision. It was not becoming worse. No ocular treatment was offered this patient. He was referred to the psychiatrist.

The following cases are further examples of obsessive states of conversion hysteria.

CASE 6.—A technician (fifth class) aged 28 was referred to the eye department because he had been told that medical discharge for his poor vision was indicated. He was said to be able to carry out the duties assigned him, and therefore his officers were desirous of retaining him if regulations permitted.

He complained of aching in the head and eyes which occurred about four times a week and usually lasted two days at a time. He had noted spots before his eyes for years. His vision had begun to blur four years prior to this examination, but he had not been examined previously and, according to his history, had never worn glasses.

Examination revealed the eyes to be normal externally and internally. In the right eye vision was 20/400 (no Jaeger) with a +4.50 D sphere, and in the left eye, 20/300 (Jaeger 7) with a +4.00 sphere.

His visual fields were normal except for relative central scotomas. He had 4 prism diopters of esophoria, 29 prism diopters of convergence and 5 prism diopters of divergence. Since he had never worn glasses, it was considered advisable to give him a full correction.

A case of this type belongs in the psychosomatic group, but the obsessive or hysterical character of the poor vision was so marked that it outweighed the large refractive error. One mistake in handling this patient was made by the person who told him before ophthalmic consultation was obtained that he was to be discharged from the Army. The patient probably had amblyopia ex anopsia of his right eye, but the poor vision in his left eye should have improved with glasses. After two months of trial of glasses, observation and reassurance and a reexamination of his eyes for evidence of progressive visual loss or increasing size of scotomas, he was referred for psychiatric treatment.

No change in his vision was obtainable with any lenses. Although he was more comfortable with them at times, no evidence of malingering was uncovered, although several examiners suspected a variable amount.

CASE 7.—A healthy young soldier, a mechanic of 19 years, was hit on the head by the tip of an airplane wing. It was a mild blow, occurring as he lifted his head after bending over. He was not stunned, nor did he report to the physician, but two weeks later he suddenly suffered an attack of blindness, which lasted an hour. Similar attacks occurred with increasing frequency. He was hospitalized, transferred several times to other hospitals and finally discharged from service because of these attacks of blindness. They could be brought on by a gentle bump on his occiput. Jarring the cranium in any other way would not bring on an attack, but if anything or any one bumped his occiput even slightly, he would suffer an attack of blindness.

These spells came on whenever the patient was struck on the occiput during his stay in the hospital, but after his discharge he was able to work without difficulty in a subdepot at an air field. He retained the fear that if he received a blow he would go blind, but in nearly a year no complaint was made. This shows

that his spells of blindness had been motivated by a desire to get out of the Army. In other words, they served a purpose, and on that basis they were classed as hysteria.

Ophthalmic examinations, including examinations of the visual fields, always gave completely normal results, whether performed at the patient's original station or at other stations.

PSYCHOSOMATIC OCULAR DISORDERS

The dividing line between the neuroses and the psychosomatic states is not a straight and narrow one. The group of cases of the latter condition is composed of those in which there was evidence of (1) psychoneurosis (frequently an anxiety state) and (2) ophthalmic abnormality on examination.

Too many eyes have been lost as a result of chronic simple glaucoma to permit one to lose sight of the fact that a pathologic condition in the eye often does not give rise to symptoms. A diagnosis of psychosomatic state is not tenable without complete ophthalmic examination. The limits of ocular pathology and the classifications of ocular disease are well defined. Included among pathologic abnormalities are those of pathologic physiology, such as divergence excess and divergence weakness.

The complaints of the patients with psychosomatic disorders were similar to those of patients who had only an ocular neurosis, but the examinations revealed a pathologic condition. In some patients one eye had been removed because of injury or disease. The other eye gave occasion for ocular complaint and yet on examination was found to be within normal limits. A one-eyed person cannot be classed as normal. The remaining eye may be subjected to strain because it is an only eye, and the psychic trauma of the loss of an eye makes the patient unduly sensitive to symptoms in the remaining eye. In these patients all the etiologic factors for a psychoneurosis were present in addition to an actual pathologic condition—the loss of an eye. Other patients in this group had had operations for strabismus, usually with good results, but they had frequent headaches, and the weaker eye gave them occasional pain.

In this group are the patients with muscle imbalances, for example, a man with divergence weakness who has orthophoria for near vision and 7 prism diopters of esophoria for distance; vision was 20/15 in each eye, and refractive error +0.50 D cyl in each eye. Such a person may well display physical symptoms, but there is frequently an overlay of neurotic symptoms. A case was included in this series in which divergence excess was associated with impending

divergent strabismus and exophoria of 14 prism diopters. Refraction showed that for vision of 20/15 the following corrections were required: right eye, +0.25 D sph \supset +0.25 D cyl, axis 10; left eye, +0.50 D sph \supset +0.25 D cyl, axis 175. In this group are also found the large refractive errors, for instance right eye, —14.00 D sph and left eye, —14.00 D sph —1.00 D cyl, axis 180, or right eye, —1.75 D sph \supset +4.00 D cyl, axis 115 (vision 20/20) and left eye, —3.00 D sph \supset +6.50 D cyl, axis 75 (vision 20/40). A person with this error in refraction would be unusual indeed if he did not have ocular complaints. Without a refraction he might be termed a "gold brick." After the refraction knowledge of his error requires that allowances be made for deficiencies in vision.

Patients with deficiencies in fusion are included in this group. A patient, aged 26, with alternate suppression and with no other abnormality evident on examination, stated that he could not get along without glasses whose strength was +0.37 D. What oculist could say that this conviction had a purely neurotic basis? The weight of the neurotic symptoms must be evaluated, so must the evidences of pathologic change. Patients with true and permanent hyperphorias make up a good percentage of this group. They almost all have headaches and blurred vision. They get some relief from vertical prisms if they will wear them, but the ocular symptoms persist.

Patients with anisometropia and aniseikonia also belong in this group. They have real refractive errors but are constantly inefficient in their work because of ocular discomfort.

CASE 8—A soldier aged 23 was operated on in the Army for divergent strabismus. A 10 degree over-correction was evident. The patient stated that he had been told he did not require glasses because one eye was amblyopic. He came in requesting further surgical treatment. He was in a mild anxiety state, and because of this operation was not considered advisable. In order to put off operation, a complete ophthalmic examination was made.

The findings were significant, but the most important factor obtained from the examination was the patient's confidence and cooperation. It was found that his refractive error was right eye, +4.00 D sph \supset +1.25 D cyl, axis 80 (vision 20/800), left eye, +1.50 D sph \supset +0.50 D cyl, axis 75 (vision 20/30). We convinced him that all he needed was glasses. His anxiety cleared up greatly, and after he had worn the full correction for two months, his eyes became grossly parallel.

CASE 9—A private aged 21 complained of headaches and burning eyes. He stated that he was chiefly concerned because of attacks of blindness in his good eye, which occurred about four times a week. At these times he lost half the vision in his good eye, usually the upper half, he could see the lower halves of objects during these episodes. One of these attacks had recently occurred in the morning in the barracks, another, while he was driving his car.

He was studied especially from the point of view of vascular spasm. Even when he was given vasodilating drugs the attacks occurred. He did not seem to recover any sooner after inhaling amyl nitrite. The macular vessels in his good eye were always observed to be wide and normal.

The vessels in the amblyopic eye were slightly attenuated, although no evidence of vascular spasm was noted. Roentgenograms of his ocular foraminae were normal, as were roentgenograms of his skull. Frequent examinations of his visual fields showed only slight enlargement of the blindspot shortly after these attacks. The altitudinal anopsia was never demonstrated by examination of the visual fields, although he reported to the clinic within ten minutes after having one of his spells.

Ophthalmoscopically the nerve heads were entirely normal. Refraction revealed the following error: right eye, +0.50 D sph (vision 20/20), left eye, +4.50 D sph \perp +3.50 D cyl, axis 100 (vision 20/400).

He stated that the loss of vision in his left eye was due to an accident in childhood in which he had injured that eye with a wire. No evidence of a perforation was seen in the cornea, the sclera or the retina. His poor vision was attributed to amblyopia ex anopsia, a conclusion which was borne out by a typical wide field with a normal blindspot but with a central scotoma.

When he was assured that his complaints had a nervous basis and that he was not going to lose his good eye, he showed gradual improvement. He finally went for eight months without any spells of blindness. His only ocular treatment was a full correction for the refractive error.

TREATMENT

As has been stated, patients with ocular complaints fall within one of three groups: (1) patients with simple neurosis, (2) patients with psychosomatic conditions and (3) patients with strictly organic disorders. The symptoms of the three groups may be identical. None of the patients can be treated until after careful and complete ophthalmic examination of the external eye, the muscular balance, the ocular fundus and the visual field, followed by cycloplegic refraction and often postcycloplegic study in patients under 40.

There is no routine simplified form of treatment for any of these three groups of patients. For patients with the anxiety type of neurosis with absolutely normal ocular findings the treatment is one of reassurance by the ophthalmologist. Relaxation of the ciliary mechanism is a powerful sedative to the overactive autonomic system of some of these highstrung patients. In the event of persistently recurrent symptoms the patient must be referred to the psychiatrist.

There are two equally poor methods of treatment used in cases of ocular neurosis in which the neurosis is not properly evaluated:

One extreme of poor treatment is illustrated in the case of a patient with simple myopic astigmatism who was told by his optometrist in civilian life that he would have been blind in another

three months if he had not been fitted with glasses. The anxiety state, of course, fed on this fear. Complete ophthalmic studies revealed vision of about 20/40 with correction during the state of anxiety tension, but at other times of 20/20. Glasses were necessary for the correction of the myopia, but psychotherapy in the form of a discussion of his condition was most important.

The other objectionable method of treatment is that of labeling such patients malingerers and considering them deserving of disciplinary action. The stigma of being classed as a malingeringer adds to the anxiety state. The feeling that some disease is present, though undiagnosed, also increases the anxiety.

The subjective findings here resemble those in many other ocular diseases. A complete ophthalmic examination is always indicated as the primary diagnostic step, and also as a foundation for the proper therapeutic approach. A general physical examination may be indicated if suspicion is aroused concerning actual organic disease or focal infection. It is a serious mistake not to recognize pathologic conditions in these patients. The patient must be told gently but frankly that his symptoms are without organic foundation. If he is inadvertently given glasses or eye drops are prescribed to help clear up the spots, the neurosis persists and usually is aggravated. Most of these persons have a high order of intelligence and insight and respond well to therapy of the chronic anxiety state, but eye drops will never cure the spots before their eyes, and glasses only "make them see the spots better."

These patients need reassurance, and they must be taught to have insight into their own problems. Over the course of years an annual physical or ophthalmic examination is advisable. Often an anxiety neurosis may be kept in the early stages by proper handling. If the neurosis is improperly handled or the patient subjected to stress beyond his capacity to sustain, the condition will go on to anxiety with exhaustion, or even to severe acute anxiety.

In treatment of hysteria and the obsessive state, ophthalmic examination is necessary to rule out organic disorders, but when this has been done, the patient should be referred to a psychiatrist.

In cases of the anxiety type of neurosis with a small refractive error it is necessary to evaluate the degree of anxiety as well as the degree of refractive error. Often a patient with this type of neurosis does well after a frank disclosure of the neurosis, and he often will agree that he recognizes his nervous temperament. In addition, correction of the refractive error is often an aid in

relieving the patient of some of his symptoms. Most of the patients with an anxiety neurosis received no glasses unless they stated that they could not get along without them. In some of these persons the use of glasses amounted to an obsession. It is impossible to make it a rule to correct only errors of 100 D or over or to draw any other arbitrary line on one side of which symptoms are considered to have an organic basis and on the other side of which they are thought to be psychoneurotic.

In dealing with large refractive errors of the hypermetropic type, should the psychoneurotic patient be given a full correction for an error which in a normal patient would be corrected by only 50 per cent of the cycloplegic findings? Here, again, it is impossible to make a fast rule.

It has been a common procedure to correct smaller errors in private practice than in the more socialized Army practice. More time is available and is required in treating the private patient. The decision rests with the refractologist, and an important fact to be considered is the actual state of the accommodation. In cases of less than average accommodative power more correction is indicated. Duane's table of average accommodative power is an important adjunct to the Prince rule. On the assumption that fatigability is a finding and a symptom of neurosis, the full correction of hypermetropic refractive error has considerable weight in its favor.

It has been our practice to correct all cylindric errors over 0.50 D and to correct myopia fully.

Many patients with large refractive errors come in for examination without any ocular complaints. I have never seen a neurotic patient with a large refractive error which gave him no symptoms. Most of the patients with neuroses have small refractive errors or orthometropia.

Among the patients with neuroses one encounters occasionally a variable hyperphoria. It varies from day to day and also varies with the administration of a cycloplegic. It has been our practice not to give vertical prismatic correction to any patient unless the hyperphoria remained constant. These patients were normal in regard to function of the ocular muscles. None of them showed even mild paresis of extraocular muscles. Do these patients belong in the neurosis group or in the psychosomatic group? The overactive autonomic nervous system may possibly be the cause of the variable hyperphoria, as with cardiac neuroses there is sometimes tachycardia or irregular rhythm.

Orthoptic treatment of such patients has much in its favor providing the patient understands his underlying neurosis. Prismatic glasses are not to be considered.

The treatment of neurosis does not include surgical intervention. For patients with psychosomatic states with a considerable psychic element an elective surgical procedure is contraindicated. In these patients temporary improvement is often seen after an operation, but the neurosis recurs later, to make the physician regret that an operation had ever been performed. These patients do best with medical treatment of their ocular defect and with psychiatric consultation.

ELECTRON MICROSCOPIC OBSERVATIONS ON BACTERIOLYSIS PRODUCED BY LYSOZYME OF TEARS

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Lysozyme is a substance in tears, described by Fleming¹ in 1922, which has a strong lytic action on certain organisms. It is also found in nasal mucus and in saliva, but it is especially abundant in egg white, tears and leukocytes.

Lysozyme is characteristically a ferment. It is water soluble, will not pass through a semi-permeable membrane and is destroyed by boiling water but not by light or drying. Its optimum action in a neutral medium is attained at 56 to 60°C.

Lysozyme even in high dilutions destroys many saprophytes of the air and is, therefore, thought to have the function in the eye of keeping the conjunctival sac free from atmospheric organisms. The significance of lysozyme for pathogenic organisms is debatable,² but Ridley³ maintained that it does prevent the growth of some organisms.

For further details on the lytic principle of tears, the reader is referred to the works of Fleming,¹ Fleming and Allison,⁴ Ridley,⁵ Wolff,⁶

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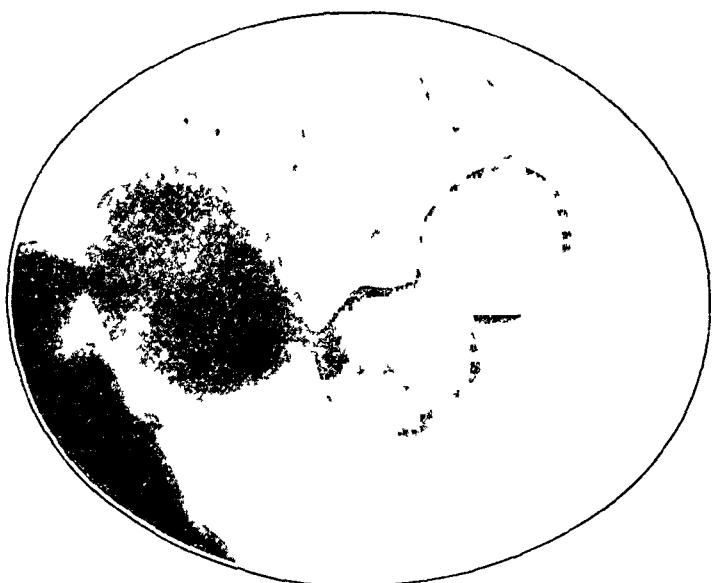


Fig 1—Normal appearance of the cocci (from air) in saline solution $\times 19,400$

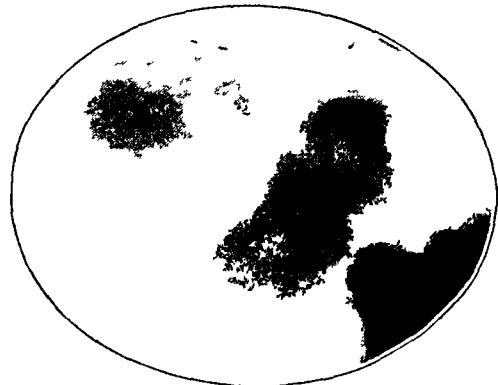
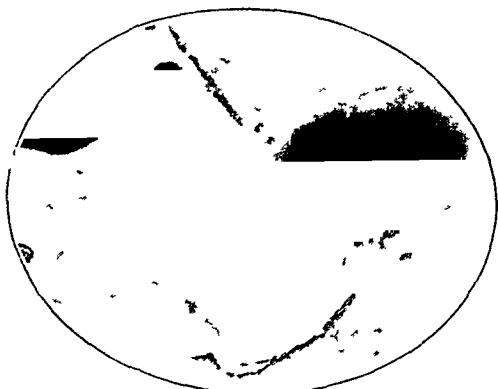


Fig 2—Cocci in the first phase of lysis with lysozyme $\times 19,400$

Nakamura,⁷ Andersen,⁸ Hallauer,⁹ Čavka and Prica,¹⁰ Calle¹¹ and Venco^{2b} and Caselli¹¹

Lysozyme differs from bacteriophage in that it is not self reproductive and is not used up during the process of lysis. The spontaneous reproduction of bacteriophage is evident by its spread through a bacterial culture as shown by the clear spots on the surface of the culture. Lysozyme also differs from bacteriophage in that it is not specific for living organisms, as is bacteriophage.

Ruska's recent observations on bacteriophage with the electron microscope have shown that the bacteriolysis is produced by the agent of the Twort-d'Heurel phenomenon. These recent

lysozyme with that of bacteriophage. Further studies in this field, such as electron microscopic observations on the behavior of aging in organisms and on some other forms of lysis (distilled water, bacteriolysis and peptic digestion), have not been possible because the electron microscope of the Superior Institute of Public Health was, in the first days of October 1943, taken to Germany by order of the German military authorities.

TECHNIC

We were unable to obtain strains of *Micrococcus lysodeikticus*, which Fleming isolated from the air and which is relatively sensitive to lysis. We used, instead, two strains of gram-negative cocci of the sarcina type, which produce a pink-yellow pigment

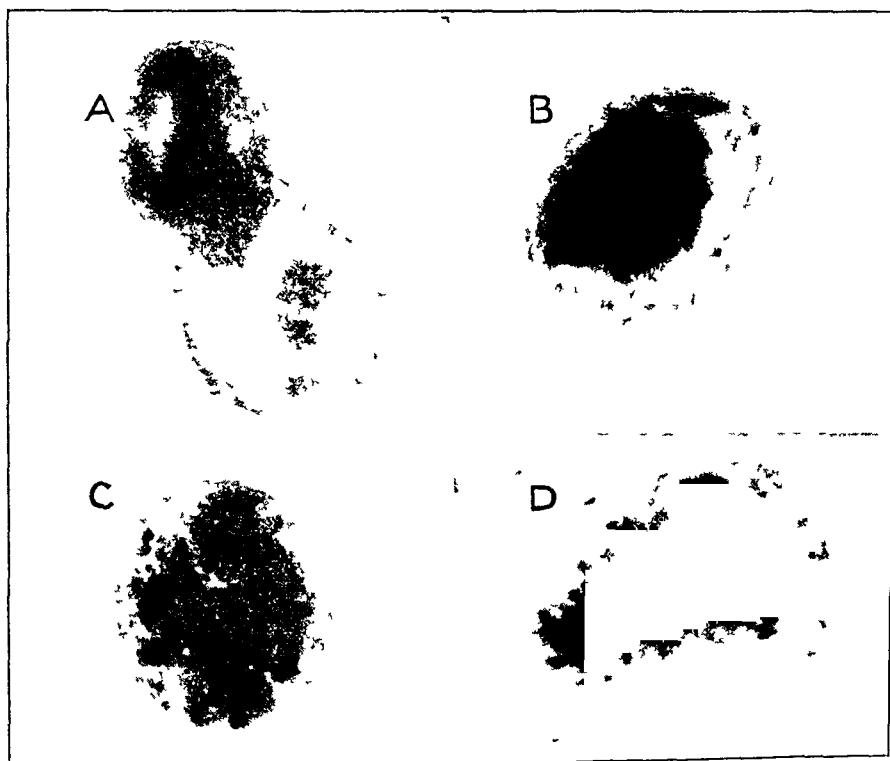


Fig 3.—Cocci in the second phase of lysis with lysozyme. A, $\times 18,200$, B and C, $\times 19,400$, D, $\times 18,200$

observations induced us to make a similar study on lysozyme with the electron microscope so that we could compare the bacteriolytic action of

(fig 1). These were isolated from the air and were particularly sensitive to the action of lysozyme.

Twenty-four hour agar colonies of these organisms were emulsified in tears diluted with isotonic saline solution in proportions of 1:50 and 1:200. Tears were obtained by mechanical irritation of the conjunctiva. The bacterial emulsions were mixed with tears and incubated in a test tube at 37°C. Samples were taken at different times, from fifteen minutes to three hours, and the degree of lysis was determined. As a control, an emulsion of organisms was used without tears. As soon as the sample was taken from the incubator, a few drops of fixative in the form of a 10 per cent concentration of solution of formaldehyde U.S.P. or of 1 per cent osmic acid was added. The fluid in the test tube was centrifuged at a rate of 10,000 revolutions per minute for twenty seconds, the supernatant fluid withdrawn and the sediment washed with distilled water. This process was repeated three times. The washed sediment was then examined with the electron microscope.

7 Nakamura, O. Ueber Lysozymwirkungen, Ztschr f Immunitätsforsch u exper Therap **38** 425, 1923.

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9 Hallauer, C. Ueber das Lysozym, Zentralbl f Bakt (Abt 1) **114** 519, 1929; Klinische und experimentelle Untersuchungen über dem Lysozymgehalt in Bindegewebsack u in der Tränenflüssigkeit, Arch f Augenh **103** 199, 1930.

10 Čavka, V., and Prica, M. Ueber Lysozymwirkung in normalen und pathologischen Augensekreten, Arch f Ophth **121** 740, 1929.

11 Caselli. Ricerche sulla bacteriolisi Dimostrazione dei germi dopo la lisi da lisozima, Boll d Ist sieroterap milanese **22** 336, 1943.

RESULTS

The following three successive phases of lysis produced by lysozyme could be identified with the organisms used.

In the first phase there was a rarefaction of the bacterial protoplasm. This was incomplete and

In the second phase the protoplasm became greatly fragmented, especially at the periphery, and showed particles of various sizes. In some cases these were placed close to the bacterial membrane, like the beads of a rosary. The organism tended to swell, a phenomenon previously

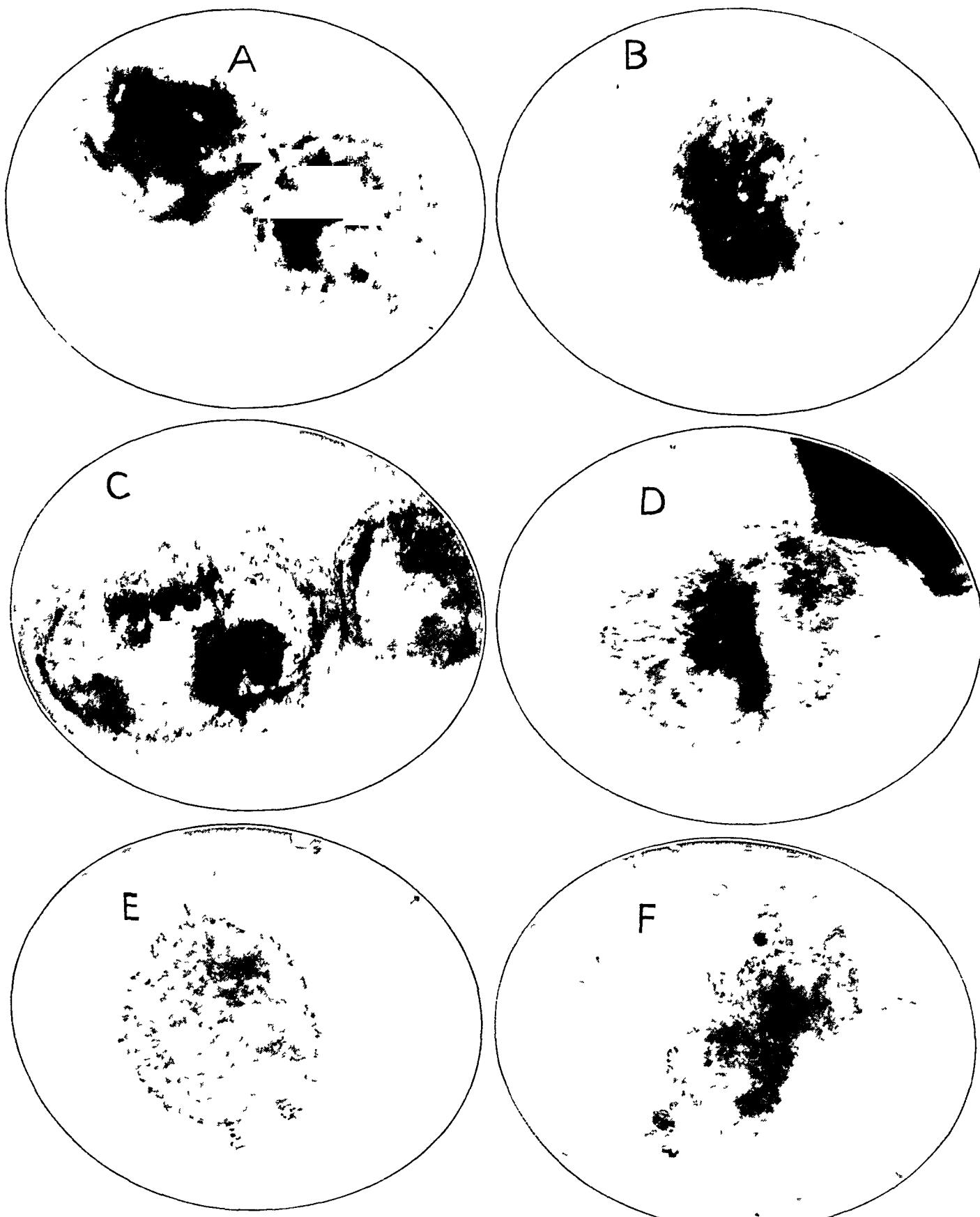


Fig. 4.—Cocci in the third phase of lysis with lysozyme. *A* and *B*, $\times 18,200$; *C*, *D*, *E* and *F*, $\times 19,400$

not uniform. Areas of thinning were clearly visible at the periphery of the bacterial body (fig. 2).

observed by Fleming, the bacterial membrane became demarcated and seemed intact, and a

transparent space appeared below the membrane (fig 3)

In the third phase the fragmentation of the protoplasm had advanced to total plasmolysis. The body of the bacteria had swollen to various degrees, being extreme in some and only moderate in others (fig 4). The sac formed by the bacterial membrane was intact and became almost transparent. It contained amorphous protoplasmic residues (figs 4 D to F).

In none of the three phases was it possible to observe protoplasm passing out of the bacterial membrane or dehiscence of the latter. But the membrane did not have a normal appearance. In the more advanced stages of lysis it often had a characteristic shagreen appearance. We did not observe internal protoplasmic residues, a fact which suggests the presence of a central nuclear substance more resistant to the lysis. In none of

lysozyme is a teinent and is clearly different from bacteriophage. This observation is consistent with the hypothesis that bacteriophage is a true living organism.

There are morphologic differences in the bacterial body dissolved by bacteriophage and that dissolved by lysozyme. In the lysis of bacteriophage there is no evident fragmentation of protoplasm, as is evident in the photographs here reproduced and in those of Ruska. The bacterial membrane apparently remains intact with both agents, although there may be some change in its permeability, as has been previously observed with the action of bacteriophage.

Sulfonamide compounds, on the other hand cause dihiscence of the bacterial membrane, with escape of altered protoplasm (fig 7), a phenomenon lacking in the action of lysozyme. The action of sulfonamide compounds has been studied by Gartner.¹²

Aging of the organisms also produces alterations in the bacterial protoplasm. We were unable to study the aging process in the two strains of cocci employed in our studies with lysozyme. We have, however, noted previously in other organisms that the granular fragmentation observed in the bacteriolysis produced by lysozyme does not take place in old organisms; instead, the protoplasm tends to become uniformly transparent while inside the bacterial body, and the nuclear bodies (fig 8) may then be distinguished (third stage of Piekarski and Ruska). The photographs show spontaneous lysis in old cultures of photobacterium (*Coccobacillus piekarskii*).

The membrane appears intact and the protoplasm presents characteristic granular fragmentation inside the bacterial body or some filamentous forms and a nucleus-like mass of undetermined significance. Since the organisms swell, the exact mechanism of action of lysozyme on the organism is not easy to explain. It is possible that the permeability of the bacterial body is altered, allowing the absorption of water by the bacterial protoplasm. It is also necessary to assume that the membrane is or becomes permeable to lysozyme.

The conclusions drawn from our investigation are clearly opposed to those of Caselli.¹¹ According to this author, the disappearance of the organisms after a specific lysis is an artefact, since it is possible to render them evident under appropriate conditions such as prolonged staining or the addition of certain chemical substances to

¹² Gartner, K. Die Sulfonamidwirkung im Lichte der Fluoreszenz und Elektronenmikroskopie, Zentralbl. f. Bakter. (Abt. 1) **150** 97, 1943.

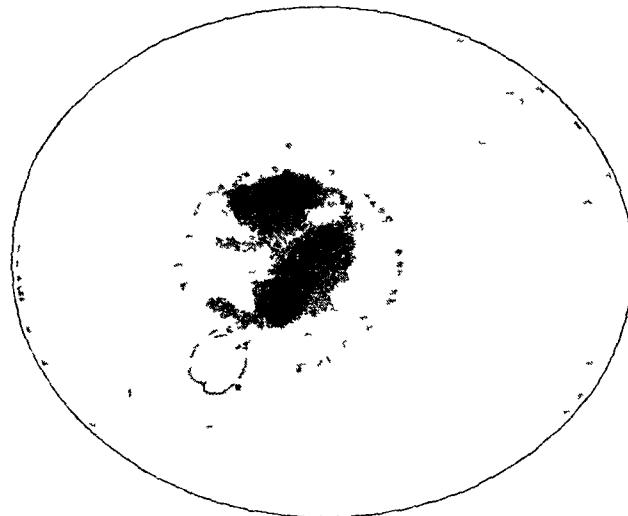


Fig 5.—Bacteriophagia of a coccus, which appears surrounded with bacteriophage bodies.

the phases were any corpuscular elements found outside the bacterial membrane, such as are observed with lysis produced by bacteriophage.

The process of lysis was not uniform in all the bacteria. Only after several hours was it complete for all the organisms. After thirty minutes bacteria in the last stages of lysis were found adjacent to others which were still intact. There were no consistent morphologic differences in the organisms fixed with the solution of formaldehyde and those fixed with osmic acid.

The conspicuous difference in lysis produced by lysozyme and that produced by bacteriophage was the absence of the round or cylindric bodies found outside the bacterial body with bacteriophage and considered by Ruska as living elements (figs 5 and 6). The absence of these forms with lysozyme confirms the idea that

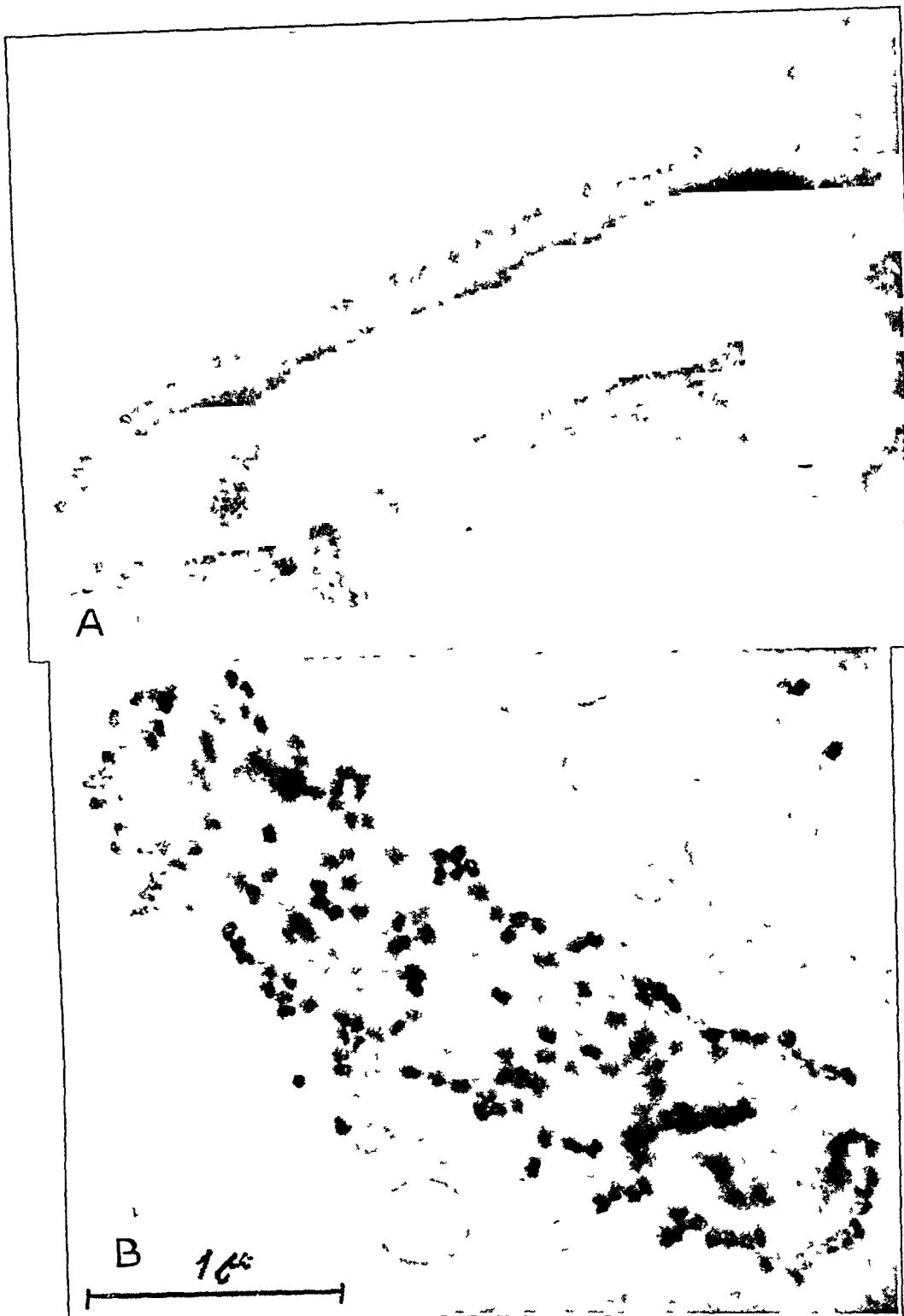


Fig. 6.—Bacteriophagia of *Eberthella typhi*. A, $\times 30,500$, B (reproduced from Ruska), 31,500

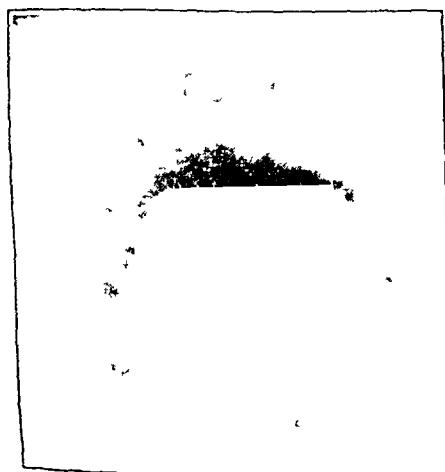


Fig. 7.—*Staphylococcus aureus* undergoing lysis with a sulphonamide drug (from Gartner¹²) $\times 38,000$

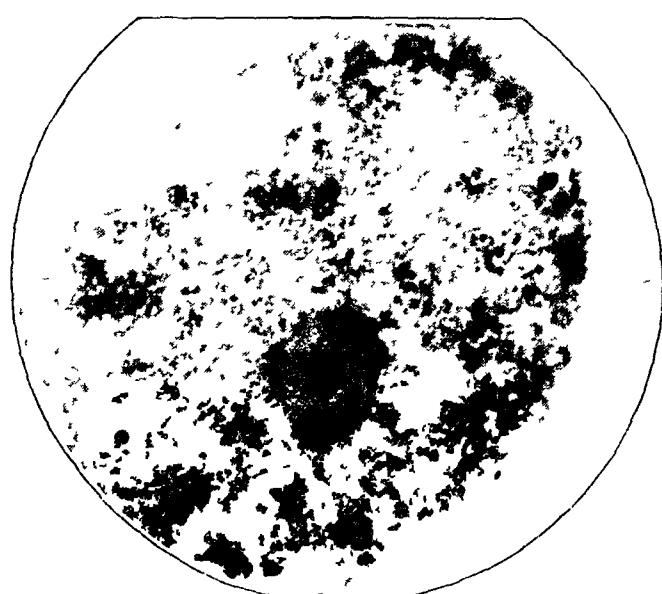


Fig. 8.—Spontaneous lysis of an aging organism (*C. pierantonii*)

the suspension According to Caselli, the apparent disappearance of organisms is actually due to the modification of their refractive indexes, rendering them indistinguishable with the ordinary microscope from the medium in which they are suspended But the pictures obtained with the electron microscope, which records the density of objects, shows that Caselli's opinion is not tenable

Under the action of lysozyme the bacterial body is actually dissolved and only the altered cell membrane persists If this membrane is treated extensively, it becomes colored and gives the picture of a destroyed organism, and this is what Caselli observed This change is evident from Caselli's own results obtained by centrifugation of the suspension of disintegrated organisms The sedimentation of organisms suspended with lysozyme is evidently due to the fact that they are not real organisms but only the residual membranes, which are lighter than the entire organisms

Our observation of the morphologic integrity of the bacterial membrane of organisms treated with lysozyme is, however, consistent with that of Boasson,¹³ who examined stained organisms in the dark field He found that the bacterial membrane is not destroyed by lysozyme but becomes permeable to protoplasm We cannot agree, however, with the expressed opinion that a swelling of the bacterial body, previously observed by Kigasawa, is lacking or that the swelling of the bacterial membrane is due to a mechanical artefact, which occurs when the smear is made

SUMMARY

Successive morphologic stages in the lysis of certain organisms with lysozyme were studied by means of the electron microscope

Prof D Bocciarelli, of the Physical Laboratory of the Superior Institute of Public Health, furnished technical help for the work with the electron microscope

13 Boasson, E H Bacteriolysis by Lysozyme, *J Immunol* **34** 281, 1938

PENICILLIN THERAPY OF INFECTIONS OF THE VITREOUS

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The distribution and depletion of penicillin after intravitreal injection into the rabbit eye, as well as the irritation and damage caused by the drug, were described in previous papers.¹ The therapeutic effect of such treatment was studied on an experimentally induced staphylococcal infection of the vitreous and was compared with that observed after similar therapy with sulfonamide compounds. One or two injections of a solution containing 2.5 mg of sodium penicillin per cubic centimeter were given.² Although the penicillin was not titrated according to the Oxford method, it was estimated that this fraction had an approximate activity of 1,000 Oxford units per milligram.

These studies established the necessity for further investigations to determine the extent to which dosage could be reduced and damage confined to a minimum without curtailing the therapeutic effect. For this purpose, experiments were conducted on infections of the vitreous with a mannitol-fermenting strain of *Staphylococcus aureus* and a strain of *Diplococcus pneumoniae* type III. In view of the practical aspect of the direct injection of penicillin into the vitreous, it was advisable to use commercial preparations of the drug.³

PRELIMINARY EXPERIMENTS

In preliminary investigations the toxicity of various dilutions of sodium penicillin obtained from two pharmaceutical companies was tested.⁴

This study was supported by the Knapp Memorial Foundation.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

1 von Sallmann, L., Meyer, K., and Di Grandi, J. Experimental Study on Penicillin Treatment of Ectogenous Infection of the Vitreous, *Arch Ophth* **32**:179 (Sept) 1944. Dunnington, J. H., and von Sallmann, L. Penicillin Therapy in Ophthalmology, *ibid* **32**:353 (Nov) 1944.

2 The penicillin was extracted and highly purified in the laboratory of Dr Karl Meyer.

3 This investigation was reported on in abstract at a meeting of the New York Ophthalmological Society on Nov 13, 1944.

4 The penicillin was provided by the Office of Scientific Research and Development from supplies

As a rule 50 to 500 Oxford units of sodium penicillin in 0.1 cc of solution was injected into the vitreous. With this amount of fluid, withdrawal of aqueous was avoided, otherwise the technic was the same as that described in former publications.¹ The eyes were examined regularly with the ophthalmoscope and the slit lamp and were usually removed for histologic study after seven weeks. A few of the rabbits succumbed to the summer heat of last year, and their eyes were enucleated as soon after death as possible.

Twenty-six eyes of chinchilla rabbits were studied. The clinical and histologic observations are presented in table 1. A traumatic cataract was accidentally produced in 2 eyes by injury of the posterior capsule with the needle. Fine deposits in the anterior part of the vitreous were frequently visible with the slit lamp. Both eyes of the only rabbit which had been given injections of 0.2 cc of the solution, after withdrawal of aqueous, showed moderate diffuse cloudiness of the vitreous four days later, but the condition could not be observed longer because of the intercurrent death of the animal. Slight edema of the retina in an area adjacent to the lower border of the optic disk was noted in 2 eyes which had received 250 and 500 Oxford units respectively. Histologically 3 of the 26 eyes presented pathologic changes in the retina consisting of isolated areas of atrophy or degeneration not exceeding $\frac{1}{2}$ disk diameter. Two of these globes had been given injections of 250 Oxford units of penicillin from one of the pharmaceutical companies, the third eye had received 500 Oxford units from the second source. The vitreous in 2 eyes contained a small number of inflammatory cells.

A comparison of the published results of toxicity experiments with purified fractions of penicillin of a similar concentration, prepared in the laboratory of Dr Karl Meyer, and observations in the present series showed in the latter a considerably lower incidence and lesser extent of retinal lesions. Lenticular opacities were absent

assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council

in the present series except in the eyes with traumatic cataract, and the inflammatory changes in the vitreous were negligible. Variations in the nature of the samples of penicillin, the alcohol content and the greater amount of fluid used in the injections in the first study may have contributed to the differences in the results of the two series. In the present study the infrequent occurrence of degenerative changes in the retina was also in contrast to the regular appearance of chorioretinal atrophy described by Leopold and Scheie,⁵ after intravitreal injections of various microcrystalline sulfonamide compounds and reported later by workers in this laboratory after similar injections of sodium sulfacetamide. In view of the observations reported here on the use of commercial sodium penicillin, theoretic objections to intravitreal treatment in cases of exogenous infection of the posterior segment are further invalidated.

TABLE 1.—*Damage to Lens, Vitreous and Retina After One Injection of Commercial Sodium Penicillin in Vitreous of Normal Rabbits*

Source of Penicillin	Oxford Units in 0.1 cc	No of Eyes Observed		Lens		Vitreous		Retina	
		For 7 Weeks	Less Than 2 Weeks	Clear	Traumatic Cataract	Clear	Exudate	Normal	Localized Atrophy
Company A	100	4	2	6	0	4	2*	5	1
	250	2	2	3	1	4	0	2	2
Company B	50	4	0	3	1	4	0	4	0
	100	2	2	4	0	4	0	4	0
	250	4	0	4	0	4	0	4	0
	500	2	2	4	0	4	0	4	0

* Animals received 0.2 cc after withdrawal of aqueous

STAPHYLOCOCCIC INFECTIONS OF THE VITREOUS

The value of commercial sodium penicillin when injected into the vitreous in various concentrations was first studied with staphylococcic infections of the posterior segment of the eye. The same mannitol-fermenting strain of *Staph. aureus* used in former experiments¹ was selected for inoculation of the eyes. Its sensitivity to penicillin was similar to that of the Oxford test strain that is, 0.01 Oxford unit per 0.2 cc prevented the growth of a 10^{-2} dilution of the culture.

Technique.—A destructive infection was always produced by injecting 0.05 cc of a twenty-four hour broth culture in a dilution of 10^{-5} . The treatment consisted of one intravitreal injection of 0.1 cc each of solutions containing 500, 250, 100, 50 and 10 Oxford units respectively of sodium penicillin. The dilutions were made steriley in a 0.9 per cent solution of sodium chloride with preparations of sodium penicillin from three pharmaceutical companies. The ex-

perimental procedure was otherwise as described in previous papers. A time interval of eight hours was selected in all experiments for uniformity. A sufficient number of infected control eyes did not receive any treatment. In general the animals were under observation for five to nine weeks, but 25 per cent died of the summer heat. Clinical examinations with the slit lamp and the ophthalmoscope were made regularly during the period of observation, and the necessary histologic study of the globes with various stains completed the record except for the animals which died unexpectedly and could not be autopsied shortly after death. The course of the infection, the result of the treatment and the histologically observed damage were surveyed and the data tabulated in each instance.

Results.—The preparations of penicillin from the different sources were almost equally effective, so that it was unnecessary to record the results separately. In this series, 84 eyes were infected, of which 24 were untreated controls. The inflammation in the control eyes always led to phthisis bulbi. Twelve of the 60 treated eyes

were removed early because of the incidental sickness or death of the animal. Despite the short period of observation in these experiments, the results could be evaluated with probability, since the course of the infection in the first few days was prognostically significant.

In the first week the inflammation of the treated eyes involved the anterior segment as well as the vitreous space. Many cells, plastic and fibrinous exudate, an intense flare in the aqueous and pronounced or extreme swelling of the iris characterized this stage. The vitreous was diffusely cloudy and the fundus was obscured, but a red reflex could usually be obtained. In the second week the inflammatory changes regressed and the anterior chamber regained an almost normal appearance. Although the opacities in the vitreous became less diffuse, strands of exudate generally remained during the subsequent weeks. A white mass of exudate was often observed in the lower periphery. Its resorption took several weeks, and a remnant often covered the retina in the form of a gray veil. In later stages involvement of the retina was more fre-

⁵ Leopold I H, and Scheie, H G. Studies with Microcrystalline Sulfathiazole, Arch Ophth 29:811 (May) 1943.

quent than in the series described in former papers. There was attenuation or distortion of the medullated nerve fibers or disappearance of the fine marginal striation of these fibers, and in a few eyes a partial or total retinal detachment was noted. Cataractous changes in the lens were noted clinically in 25 eyes. In 5 eyes the cataract was definitely traumatic, and in the remaining eyes injury with the needle could not be excluded. Clinical observations showed that the infection was checked in all but 3 of the treated eyes.

The extent and nature of the damage caused by the infection in the successfully treated globes could be ascertained by histologic examination. The lesions were divided into opacities of the lens, presence of inflammatory cells in various parts of the eye and organized strands and membranes in the vitreous which caused traction folds of the retina or retinal detachment.

Around the disk and produced traction folds (small in 23 eyes and large in 11 eyes). Extensive retinal detachment, also due to traction, was noted in 4 eyes. Occasionally these strands pulled the optic nerve inward. The remainder of the massive exudate over the surface of the retina, observed clinically, had undergone organization, with formation of connective tissue, which often produced small retinal folds near the ora serrata.

The histologic examination usually corroborated the clinical report, although slight inflammatory changes and the formation of traction folds were not always recognized with the ophthalmoscope. The presence of an abscess in the vitreous, as diagnosed clinically in the 3 cases in which penicillin failed, was confirmed in the histologic sections. These eyes had been treated with 10, 250 and 500 Oxford units of sodium

TABLE 2.—Effect of One Intravitreal Injection of Commercial Sodium Penicillin in Various Concentrations on Staphylococcal Infections of the Vitreous

Oxford Units of Penicillin in 0.1 cc	No. of Eyes Observed		Infection			Clear	Damage to *						
	5 Weeks	Less Than 2 Weeks	Definitely Checked	Probably Checked	Not Checked		Vitreous			Retina			
							Traumatic Cataract	Complicated Cataract or Infective Focus	Few Inflammatory Cells	Many Inflammatory Cells and Strands	Normal	Small Circumscribed Folds	Large Traction Folds or Extensive Destruction
10	10	0	9	0	1	4	2	4	5	4	2	6	1
50	8	2	8	2	0	5	1	2	6	2	0	4	1
100	14	4	14	4	0	12	0	6	14	4	7	7	4
250	10	6	10	5	1	7	2	6	14	1	5	6	4
500	6	0	5	0	1	3	0	2	4	1	2	2	1
	48	12	46	11	3	30	5	20	43	12	19	25	11

* Five eyes were not examined histologically.

The opacities of the lens were recognized histologically as posterior complicated cataracts in 5 eyes. Injury of the posterior capsule by the needle was identified as the cause in 5 eyes, and an infective focus in the posterior part of the lens was noted in 15 eyes. It could not be determined whether such a focus was produced by the needle during inoculation or by the spread of the infection from the vitreous.

A small number of inflammatory cells, mostly round cells, were present in the posterior chamber and in the vitreous of the majority of the eyes even in globes enucleated after eight or nine weeks. Cellular elements in various stages of degeneration were seen more frequently in Cloquet's canal, on the surface of the optic disk and on the lower half of the retina than in other areas of the vitreous space. An accumulation of these cells was noted in 12 eyes.

The most serious lesion consisted of fine strands of organized exudate in the vitreous; these strands as a rule were inserted on the retina

penicillin per 0.1 cc respectively. In general there was no convincing evidence that the extent of postinflammatory lesions depended on the dose administered except in the eyes in which the smallest dose, of 10 Oxford units in 0.1 cc, had been injected. In these eyes the signs of traction on the retina and the optic nerve due to shrinking strands of exudate were almost always present, as the data in table 2 illustrate.

PNEUMOCOCCIC INFECTIONS OF THE VITREOUS

One preparation of commercial sodium penicillin was employed in this series of experiments, in which 48 eyes, including the controls, were used. The number of the controls was limited to 10 eyes because previous experiments had demonstrated the unfailingly destructive course of this type of infection in rabbits. Septicemia and early death occurred relatively often. Both eyes of 19 rabbits, therefore, were treated, and both eyes of 5 rabbits were used as controls. In view of the sensitivity of *D. pneumoniae* type III to penicillin (growth was inhibited by 0.006 Oxford unit per 0.2 cc), the minimal dose was reduced to 5 Oxford units per 0.1 cc.

In a supplementary series, 7 eyes were treated by subconjunctival administration of 0.5 cc of a solution of penicillin containing 2,500 Oxford units. The outcome of this treatment was collated with that of intravitreal injection of a small fraction of this dose.

Technic.—The infection was produced, as in the experiments with *Staph. aureus*, by the inoculation of 0.05 cc of a twenty-four-hour broth culture of *D. pneumoniae* type III in a 10^{-5} dilution. Eight hours later 0.1 cc each of isotonic solutions of sodium chloride containing 100, 10 and 5 Oxford units of sodium penicillin respectively was administered. The procedure of the simple intravitreal therapy was modified after the first experiments by the injection of an additional small quantity of penicillin solution beneath the conjunctiva at the site of the original inoculation. This change was suggested by the spread of the infection through the extraocular tissue in the path of the needle.

Observations on the eyes with pneumococcal endophthalmitis were not extended beyond five weeks, since

chamber. The density of the opacity in the vitreous decreased, so that the fundus could be well inspected with the ophthalmoscope. This portion of the eye was normal in 9 of 10 eyes in the group in which 100 Oxford units per 0.1 cc was injected, in the remaining eye the retina had been torn with the needle, resulting in retinal detachment without inflammatory signs. Histologic examination revealed that the uvea and lens of all eyes were normal and the remnants of inflammation in the vitreous were negligible. The retina was normal in 7 eyes, and small, flat retinal folds were present in the region of the ora serrata in 1 eye. A small chorioretinal scar and the aforementioned tear of the retina in the 2 remaining eyes were obviously caused by trauma and were unrelated to the infection.

TABLE 3.—Effect of Two Types of Topical Therapy with Commercial Sodium Penicillin in Various Concentrations on Pneumococcal Infections of the Vitreous

Type of Therapy	Dose, Oxford Units	No of Eyes Observed			Infection			Damage to							
		4 to 5 Weeks		Less Than 1 Week	Definitely Checked	Probably Checked	Not Checked	Lens		Vitreous			Retina		
								Traumatic Cataract	Complicated Cataract or Infective Focus	Few Inflammatory Cells	Many Inflammatory Cells	Abscess	Normal	Small Circumscribed Folds	Large Folds or Extensive Detachment
Intravitreal injection, 0.1 cc	5 10 100	5 6 10	6 4 0	1 5 10	5 2 0	5 3 0	7 9 10	0 0 0	4 1 0	3 4 10	4 4 0	4 2 0	6 7 7	0 0 2	5 3 1*
Subconjunctival injection, 0.5 cc	2,500	1	6	0	0	7								Panophthalmitis	

* Traumatic detachment occurred.

the clinical signs of inflammation disappeared within two weeks after injection. Clinical and histologic examinations of the eyes were carried out in a way similar to that in experiments with staphylococci. In the series with subconjunctival injection, 2,500 Oxford units of sodium penicillin in 0.5 cc of 0.9 per cent sodium chloride was employed, one-half the dose being injected in the upper part and one-half in the lower part of the bulb.

Results.—In the control eyes an intraocular purulent inflammation was fully developed at the end of forty-eight hours, panophthalmitis and phthisis bulbi characterized the subsequent course. The initial signs of the acute endophthalmitis resembled those observed in the eyes with staphylococcal infections. In the first week following the treatment, however, plastic exudate was rarely seen in the contracted pupil, although the number of cells and the flare in the aqueous were often excessive. The iris usually showed moderate swelling and the vitreous a slight cloudiness, which did not completely obscure the landmarks of the eyeground.

In the second week a few cells and a moderate Tyndall sign were still visible in the anterior

Seven of the 10 eyes treated with a solution containing 10 Oxford units per 0.1 cc displayed equally favorable results, although the number of inflammatory cells in the cortical area of the vitreous and on the optic disk was greater. The period of observation on 1 of the rabbits of this group was limited to one week, when the animal died of a large metastatic subphrenic abscess. The 3 eyes of this group counted as therapeutic failures had definitely benefited from the treatment, but circumscribed purulent exudate had greatly damaged the retina.

When the dose was reduced to one of 5 Oxford units per 0.1 cc, the incidence of failures was further increased. Six of the 11 treated eyes were definitely or probably cured (table 3), and 5 were lost. Two of the rabbits which responded favorably died of septicemia in the first week. Pneumococci were grown in pure culture on plates seeded with heart blood. Histologic examination of the eyes of these animals did not disclose more than a few inflammatory cells in the periphery of the vitreous, so that the local process was considered as probably checked. The

5 globes tabulated as lost showed signs of a beneficial therapeutic effect. Exudative detachment of the retina, however, involved the lower half in 3 eyes and was total in 2 eyes.

The course of the infection in the 7 eyes which were treated by subconjunctival injection did not differ noticeably from that in the untreated controls, that is, abscess in the vitreous, panophthalmitis and phthisis bulbi developed in the rabbits that survived.

COMMENT

Three main conclusions can be drawn from these experiments on penicillin treatment initiated eight hours after vitreal infection. They slightly modify and extend the deductions made in previous papers. First, it was shown that commercial penicillin had a full therapeutic effect in concentrations which did not cause any detectable lesions of the delicate structures of the eye. Second, subconjunctival injection of concentrated solutions of penicillin resulted in complete therapeutic failure. Third, the effectiveness of the intravitreal administration of penicillin in pneumococcal infections of the posterior segment exceeded that observed in staphylococcal infections, especially in regard to the prevention of postinflammatory sequelae.

With reference to the first conclusion, it may be emphasized that previous chemotherapeutic attempts to check or influence such experimental staphylococcal or pneumococcal infections did not meet with success. Von Rotth⁶ investigated the effect of the acridine derivatives, rivanol (2-ethoxy-6,9-diaminoacridine lactate) and acriflavine, and of methenamine when given intravenously. Experimental infections of the vitreous with *Staph. aureus* and *D. pneumoniae* were not influenced by the therapy. In earlier studies in this laboratory on a similar standard lesion, intravitreal injection of sodium sulfacetamide combined with systemic therapy with sulfonamide compounds was also ineffective. Moreover, the relative toxicity of the acridine derivatives and the sulfonamide compounds as shown in vitro and in vivo precludes their injection into the vitreous space in suitable concentrations. In contrast, a full therapeutic effect was achieved in experimental infections of the vitreous with a noninjurious amount of penicillin, that is, 0.1 cc of a solution containing 100 Oxford units.

The larger size of the human vitreous and the moderate damage observed in rabbits with more

concentrated solutions of penicillin would indicate that an increase in this dose is permissible in the human eye without undue danger to the retina and lens. Whether larger doses are necessary will depend on the results of extensive clinical and histologic observations. Rycroft injected 1,000 to 5,000 Oxford units of penicillin into the vitreous in 5 patients with wail injuries without ill effect.⁷ No conclusions can be drawn from this statement, however, since histologic studies were not reported and the toxic effect cannot be evaluated in eyes with long-standing infection. In the usually less acute course of exogenous infections of the human eye, the humoral and cellular defense mechanisms may give greater support to the drug and may even permit a decrease in the minimal effective dose. On the other hand, the proved sensitivity of the infective organisms, the accurate placing of the focus and the relatively short time between the inoculation and the treatment render the experimental infection more suitable for successful topical therapy.

The treatment was not repeated in the present series, since former studies indicated the futility of continued therapy. The course of the inflammatory process after a second injection of penicillin even conveyed the impression that the endophthalmitis was aggravated. In addition, one day after the first treatment the pathologic changes in the unfavorable cases were beyond the stage at which penicillin therapy was successful in our hands. For the same reason, it was inadvisable to repeat the subconjunctival injection in the eyes with pneumococcal endophthalmitis.

Struble and Bellows reported a concentration of 1.9 Oxford units of penicillin per cubic centimeter in the vitreous fluid after subconjunctival injection,⁸ whereas little or no penicillin was detected in the experiments of this laboratory with slightly modified technic. It was desirable, therefore, to test the possible effect of such therapy on an infection produced by an organism highly susceptible to penicillin. The study was also suggested by the assertion of Dawson and Hobby⁹ that "the estimation of drug levels by necessarily crude methods give

⁷ Rycroft, B. W. Penicillin and the Control of Deep Intra-Ocular Infection, *Brit. J. Ophth.* **29**, 57 (Feb.) 1945.

⁸ Struble, G. C., and Bellows, J. G. Studies on the Distribution of Penicillin in the Eye and Its Clinical Application, *J. A. M. A.* **125**, 685 (July 8) 1944; Bellows, J. G. Penicillin Therapy in Ocular Infections, *Am. J. Ophth.* **27**, 1206 (Nov.) 1944.

⁹ Dawson, M. H., and Hobby, G. L. The Clinical Use of Penicillin. Observations on One Hundred Cases, *J. A. M. A.* **124**, 611 (March 4) 1944.

⁶ von Rotth, A. Chemotherapy of Septic Endophthalmitis. *Magyar Orvosi arch.* **28**, 252, 1927; Chemotherapy in Intraocular Inflammation, *Budapesti Orvosi Ujsag* **26**, 1153, 1928.

no information regarding the biological activity of material containing only traces of penicillin." From the complete failures of subconjunctival injections of penicillin in treatment of pneumococcic infections it can be inferred that under the conditions of the experiment low and erratic levels of penicillin were insufficient to cope with an acute infection of the vitreous. The slow diffusion of the drug in the vitreous gel and the acid milieu in acute stages of endophthalmitis probably contributed to the failure. Garrod¹⁰ demonstrated the decline in activity of penicillin with a shift of the hydrogen ion concentration to 5.5, a degree of acidity present in the infected vitreous.¹¹

The minimal effective dose of penicillin for infections of the vitreous with a strain of *Staphylococcus* of medium susceptibility was about 10 Oxford units per 0.1 cc. When the dose was reduced to this amount, the inflammation regressed more slowly than in the eyes treated with higher concentrations of penicillin, and the shrinking exudate in the vitreous was more destructive than in other series. The dependence of the clinical course of the endophthalmitis on the dose was more clearly demonstrated in the pneumococcic infections. Treatment beginning eight hours after inoculation was fully successful with a solution containing 100 Oxford units in 0.1 cc., whereas the treatment was unsatisfactory in 5 of 11 eyes with the introduction of only 5 Oxford units per 0.1 cc.

The postinflammatory sequelae, namely, strands in the vitreous, so frequent after cure of staphylococcic infections, were almost totally absent with pneumococcic endophthalmitis. In experiments now in progress it has been noted that intravitreal injection of the exotoxin from the same strain of *Staph. aureus* caused the formation of a shrinking exudate similar to that observed in the infection with the organisms. The persistent action of the toxin formed prior to the injection of penicillin may be related, therefore, to the formation of strands in the vitreous.

OBSERVATIONS ON HUMAN EYES

Experimental results were considered as a sufficient basis for treating several patients with perforating injuries and definite or probable infection of the posterior segment.

CASE 1—J. N., aged 43, was admitted to the Institute of Ophthalmology on Oct. 30, 1944, forty-eight hours after injury to the left eye, with a foreign body in the vitreous and signs of a severe intraocular infec-

tion. The lids and conjunctiva were red and edematous, and laceration of the cornea extended from the center upward to the limbus, with circumscribed incarceration of the iris. A hypopyon filled half the shallow anterior chamber, the inflammatory reaction and a traumatic cataract prevented visibility of the eyeground. Vision was reduced to light perception and faulty projection below. Dr. John H. Dunnington removed by the scleral route a magnetic, flat foreign body, 11.5 mm long and 3 to 4 mm wide, to which a web of purulent exudate adhered. Two-tenths cubic centimeter containing 200 Oxford units of sodium penicillin was injected through the scleral wound into the vitreous after the sutures were tied. The purulent material of the foreign body and the exudate from the wound were cultured on various nutrient mediums.¹²

The coagulase-positive and mannitol-fermenting strains of *Staph. aureus* which were isolated were sensitive to penicillin. Because of the involvement of the anterior chamber, penicillin was introduced iontophoretically four times during the subsequent week, and two injections of typhoid vaccine supplemented the topical therapy.

The inflammatory signs subsided gradually. Three months after the injury the eye was white and the cornea clear except for a linear scar in the upper half. A small amount of organized exudate was visible on the surface of the cataractous lens. A red fundus reflex was obtained with the ophthalmoscope, but no details of the fundus were visible. In spite of the cataract, the patient could count fingers and projected the light accurately. Examination one month later gave the same result.

CASE 2—C. K., aged 62, was admitted two days after injury to the right eye with a wooden slat. Thirty-six hours before admission the patient experienced loss of vision followed by extreme pain. At the time of admission, on Aug. 21, 1944, a perforating wound was present at the limbus above, surrounded by purulent exudate. A hypopyon and a muddy iris were seen through the steamy cornea. The pupil was contracted and drawn toward the wound. Light perception was faulty downward. The red fundus reflex could not be obtained.

On the day of the patient's admission the eye received one iontophoretic application of a solution of sodium penicillin containing 1,000 Oxford units per cubic centimeter (2 milliamperes for five minutes). On the following day, when massive exudate was seen in the vitreous through the dilated pupil, Dr. Mervyn Wheeler injected into the vitreous 0.1 cc. of sodium penicillin containing 100 Oxford units. Iontophoresis with the penicillin solution was repeated three times during the subsequent week. Systemic treatment consisted of four injections of typhoid vaccine and oral administration of sulfadiazine.

Cultures of material taken from the conjunctiva two weeks after the patient's admission were negative for pathogens. Cultures made two days later, however, showed a strain of *Staph. aureus* which was relatively resistant to penicillin. In the weeks that followed the inflammatory symptoms and signs regressed, and the exudate in the vitreous was slowly absorbed. Vision improved to 10/200 and parts of the fundus became visible, but strands of exudate still prevented examination of the disk five months after the accident.¹³

12 Dr. Devorah Locatcher-Khorazo did all the bacteriologic work on the human eye.

13 Wheeler, M. Paper read at the meeting of the New York Ophthalmological Society, Nov. 13, 1944.

10 Garrod, L. P. The Action of Penicillin on Bacteria, Brit. M. J. 1:107 (Jan. 27) 1945.

11 von Sallmann, L. Hydrogen Ion Concentration of the Vitreous in the Living Eye, Arch. Ophth. 33:32 (Jan.) 1945.

CASE 3—S P, aged 68, was operated on for cataract of the right eye on Nov 3, 1943. Small prolapses of the iris pillars were noted postoperatively. On April 3, 1944 the patient complained of heaviness of the right eye during the preceding week. On May 11 she began to see black spots, and the eye became red and painful. She was admitted on the same day, with pronounced swelling of the lids, chemosis and a purulent conjunctival discharge. Pus covered the area of the prolapsed iris. The cornea was hazy, and the anterior chamber contained fibrinous exudate. The fundus reflex could barely be seen, and vision was reduced to light perception and faulty projection. Late in the same day 0.2 cc of a solution of sodium penicillin containing 200 Oxford units was injected into the anterior chamber, after the withdrawal of aqueous fluid, and the same amount was injected into the vitreous. Cultures of the aqueous fluid revealed mannitol-fermenting and coagulase-positive *Staph aureus* and a few colonies of non-mannitol-fermenting and coagulase-negative *Staph albus*. The sensitivity of the strain of *Staph aureus* was low, as 0.25 Oxford unit in 0.2 cc was necessary to inhibit the growth of the culture. Because of the severe iritis sodium penicillin was applied iontophoretically once a day during the following week. Systemic therapy consisted in the daily administration of 100,000 Oxford units of sodium penicillin for thirteen days, supplemented with four injections of typhoid vaccine. The signs of inflammation regressed, but phthisis bulbi developed, and the eye was enucleated.

CASE 4—B F, aged 46, was admitted to the service of Dr Thomas H Johnson on Nov 14, 1944, two hours after the right eye was struck with a piece of glass. In addition to a small cutaneous wound of the brow and a subconjunctival extravasate, there were two perforating, irregular wounds, extending from the lower half of the cornea to the sclera. A small prolapse was present, and swollen lenticular matter protruded into the pupillary area. Ten hours after the accident the prolapsed iris was excised, and 0.1 cc of sodium penicillin containing 100 Oxford units was injected into the lens and the same amount into the vitreous through the scleral laceration, after the corneal wound had been closed with two sutures. Finally, a conjunctival flap was dissected and sutured to the upper portion of the limbus.

Culture of material taken from the wound prior to operation yielded a mannitol-fermenting and coagulase-positive strain of *Staph aureus*. Tests indicated average sensitivity to penicillin.

The subsequent course was uncomplicated except for atropine dermatitis of the lids. Two weeks after the injury the anterior chamber was still absent and light perception was faulty. The eye was enucleated nineteen days after injury. Histologic examination of the eyeball showed an irregular, epithelialized wound of the cornea, cataractous changes in the lens and a traumatic defect of the iris. The lens was free from inflammatory changes, and the vitreous and choroid contained only a small number of round cells. The retina and choroid were detached. The retina, which showed hemorrhages on its surface and destruction of the rods and cones due to the detachment, was otherwise normal except for a circumscribed perivascular infiltration of one vessel.

Mannitol-fermenting strains of *Staph aureus* were isolated in all cases. It is doubtful, however, whether the staphylococcus cultured from

the material of the conjunctiva in case 2 was the cause of the severe endophthalmitis. The strains isolated in cases 1 and 4 had an average sensitivity to penicillin, whereas the strains isolated in cases 2 and 3 had a low sensitivity. Topical penicillin therapy over a period of two weeks may have made the strain in case 2 relatively penicillin fast. The endophthalmitis responded surprisingly well in cases 1 and 2 in view of the advanced stage of the intraocular inflammation and the lapse of more than forty-eight hours between the injury and the treatment. Whether the additional iontophoretic and systemic treatment participated in the unexpected beneficial results cannot be ascertained. It is justifiable to assume, however, that the good effects were achieved mainly by the direct injection of penicillin into the vitreous.

The interval between the beginning of the inflammation and the injection of penicillin was unknown in case 3, but on the patient's admission the eye presented the signs of imminent panophthalmitis, the course of which was modified but not checked by the treatment. The low sensitivity of the infecting organisms to penicillin may also have had a bearing on the therapeutic failure.

The absence of any inflammatory signs in the lens and the slight reaction in the vitreous retina and choroid in case 4 indicated that the amount of penicillin was well tolerated. It is possible that the intravitreal injection of penicillin prevented the development of endophthalmitis septica (Fuchs), the existence of which was suggested by the dense perivascular infiltration of one retinal vessel.

Rycroft reported the failure of intravitreal treatment with concentrated solutions of penicillin of deep infections of the eye due to penetrating war wounds. His conclusion that such treatment does not influence the course of deep infections was based on the results in 4 cases of abscess of the vitreous, in which periods of seven, twelve, nineteen and thirty-four days respectively had elapsed between the injury and the injection of penicillin. In a fifth case, with a week old injury, the condition was described at the time of treatment as "amounting almost to panophthalmitis." In none of the eyes was the infecting organism identified, nor was a histologic examination mentioned. It seems, therefore, that these eyes were scarcely suitable for an evaluation of the therapy. It is difficult to conceive how any antibacterial agent can be expected to restore or improve the completely lost function of the eye with an old and massive purulent exudate in the vitreous. The fifth case

reported by Rycroft in which an inflammation amounted "almost to panophthalmitis," can be compared to case 3 and also to cases of experimental infections in rabbits in which the treatment was initiated too late. The response to the treatment in cases 1 and 2 of the present series indicates, however, that the twelve hour limit for satisfactory treatment of experimental exogenous infections can be extended for similar conditions of the human eye and that encouraging results can be obtained after the signs of an alarmingly severe endophthalmitis have appeared.

SUMMARY

1 Intravitreal injections of 100 and 10 Oxford units of commercial sodium penicillin obtained from various sources did not cause any noticeable damage to the retina, lens or optic nerve. The lesions caused by 500 and 250 units of sodium penicillin were negligible.

2 Staphylococcal infections of the vitreous were checked by the injection of 10 Oxford units of sodium penicillin eight hours after inoculation. The therapeutic effect was increased when five to forty times this amount was given. In a considerable percentage of the beneficially treated eyes shrinking strands of organized exudate produced traction folds of the retina.

3 Pneumococcal infections of the vitreous were arrested in all eyes when 100 Oxford units of sodium penicillin was administered eight hours after inoculation. A reduction of the dose to 5 Oxford units led to unsatisfactory results in 5 of 11 eyes. The successfully treated eyes were usually free of postinflammatory sequelae.

4 Pneumococcal infections were not influenced by the subconjunctival administration of 250 Oxford units of sodium penicillin eight hours after inoculation.

5 Two of the 3 patients with severe traumatic endophthalmitis involving the vitreous space responded favorably to intravitreal injection of penicillin despite the advanced stage of the infection and the lapse of more than forty-eight hours between injection and the first intravitreal treatment.

NOTE.—Since this study was completed, an article by Leopold¹⁴ on the intravitreal penetration of penicillin has appeared.

Dr John H Dunnington, Dr Maynard Wheeler and Dr Thomas H Johnson permitted the report of their cases.

Mrs Florence Cardenas assisted in the study
630 West One Hundred and Sixty-Eighth Street

¹⁴ Leopold, I. H. Intravitreal Penetration of Penicillin and Penicillin Therapy of Infections of the Vitreous, *Arch Ophth* 33:211 (March) 1945.

INFLUENCE OF LOCAL APPLICATION OF SULFONAMIDE COMPOUNDS AND THEIR VEHICLES ON REGENERATION OF CORNEAL EPITHELIUM

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There have appeared excellent reviews by Bellows,¹ Alvaro,² Thygeson³ and Wagener⁴ concerning the toxic properties of the sulfonamide compounds on ocular structures. Although much has been written about the toxic influence of these compounds on wound healing elsewhere in the body, only recently has consideration been given to their influence on healing of ocular wounds. Bellows considered this property in his review in June 1943. The data for these conclusions were based on the experimental work of Bellows and Gluckman.⁵ These authors concluded that locally applied sulfonamide compounds greatly delay regeneration of corneal epithelium. Berens, De Gara and Loutfallah⁶ demonstrated in 1943 that the average healing time of the wounds of the cornea treated with sulfonamide ointment or with the ointment base alone was usually greater than the average healing time of the untreated eyes. They suggested that the local use of the sulfonamide compounds be limited to cases in which chances of infection prevail. They demonstrated a more retarding effect of sulfonamide ointment on the healing of deep wounds than on that of superficial

wounds. Smelser and Ozanics⁷ reported in October 1944 that sulfonamide drugs differed in their ability to delay epithelial regeneration and that ointment preparations of these compounds did not retard epithelial regeneration as much as powders. Because of the practical importance of sulfonamide compounds in preventing secondary infection in war injuries of the eyes, as well as in civilian ocular lesions, in order that proper emphasis be given to the delay of corneal epithelialization by sulfonamide compounds, and in view of the recent interest in this subject, it seemed desirable to report some observations made in 1943.

EXPERIMENTAL STUDY

In order to evaluate properly the influence of sulfonamide preparations on regeneration of corneal epithelium it is necessary to determine the effect of ointment bases and powder bases without the addition of the drug. In the following series both of these problems were considered. Each series consisted of 6 rabbits. All the rabbits were blue-eyed chinchillas, weighing approximately 2 to 2.5 Kg. De Rotth⁸ stated that lesions produced by mechanical denudation and involving the limbus are unsatisfactory, it is too difficult to be certain that one is producing constant damage, and therefore the variations are greater. However, this was the type of lesion used by Bellows and Gluckman, and so it was employed here, with the substitution of tetracaine for cocaine anesthesia. In the first experimental series, 6 groups of 6 rabbits were used. All the corneas were stained once daily with 1 per cent fluorescein sodium and irrigated with a minimum of isotonic solution of sodium chloride, care being taken not to direct the fluid on to the corneal surface. In eyes in which any type of ointment or powder was used, applications were made five times daily.

Previous studies have shown that local application of sulfonamide compounds will barely maintain an adequate level of the drug in the aqueous in eyes with epithelium denuded if the drug is applied only every six hours in ointment form.⁹ The corneal level is higher than the aqueous level when the sulfonamide

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9 Adler, F H, Leopold, I H, Steele, W H, and Crandall, A C Unpublished observations

compound is applied locally and is, therefore, probably adequate with applications every six hours. It was thought that five applications daily would most likely insure higher levels, and so this method was used. Whenever the cornea appeared infected, the animal was discarded and a new one substituted. Four eyes in this first series were thought to be infected, as evidenced by a gray sloughing corneal infiltrate and pronounced pericorneal injection, rapidly proceeding to involvement of the remainder of the cornea and hypopyon formation. No sulfonamide-treated eye underwent such changes in this group.

The vehicles used in this first group were Friedenwald-Fuqua¹⁰, hydrous wool fat and petrolatum, 50 per cent each, Aquaphor,¹¹ and sterile calcium carbonate powder, one of the substances poorly soluble in water used by Wallace and Tiernan to prepare their buffered sulfanilamide. The sulfonamide compounds used were (1) sodium sulfadiazine, 10 per cent in hydrous wool fat-petrolatum ointment, (2) microcrystalline sulfadiazine, 10 per cent in Friedenwald-Fuqua ointment, and (3) 100 per cent buffered sulfanilamide.¹²

It is evident that by the fourth day 67 per cent of the eyes with simple denudation, 38 per cent of the eyes treated with ointment base or powder base alone and 42 per cent of the sulfonamide-treated eyes had completely regenerated. Analysis of these statistics by computation of chi square,¹³ however, indicates no significant difference in healing between eyes treated with an ointment base and eyes with simple, untreated, denudation, between sulfonamide-treated eyes and eyes with simple denudation, and between eyes treated with an ointment base alone and sulfonamide-treated eyes.

By the fifth day 92 per cent of the eyes with simple denudations, 50 per cent of the eyes treated with ointment base or powder base alone and 42 per cent of the sulfonamide-treated eyes had completely regenerated. Analysis here by

TABLE 1.—Influence of Ointments, Powders and Sulfonamide Preparations on Mechanical Denudations Involving the Limbus

Day of Regeneration	No. of Eyes Whose Epithelium Had Regenerated on Indicated Days													Incidence of Scars
	3	4	5	6	7	8	9	10	11	12	13	14	—	
Simple denudation	2	2	1			1								1
Sulfadiazine, microform, 10% in F F* ointment		4								2				
Friedenwald Fuqua ointment		1	2						1	1	1	1		2
Sulfadiazine, microform, 10% in F F ointment	2	1				1	2							
Hydrous wool fat-petrolatum base 50% each	3	3												
Sodium sulfadiazine, 10% in L P† 50% each	3	2								1				
Microcrystalline sulfadiazine powder	1			1	1	3								1
Sodium sulfadiazine, 10% in L P, 50% each	1			1	4									
Buffered sulfanilamide				3	2									2
Calcium carbonate alone (sterile)										1	2	1	1	2
Simple denudation	1	3	2						1	1	1			
Aquaphor alone		2	1											
Totals	—	—	—	—	—	—	—	—	—	—	—	—	—	
Simple denudation	3	5	3	0	0	1								12
Ointment base and powder base control	3	6	3	0	0	0	2	2	4	2	1	1		24
Sulfonamide drugs in ointment and powder base	7	8	0	5	7	4	3	1	1					36

* Friedenwald Fuqua ointment.

† Hydrous wool fat-petrolatum base.

The data from this first series of experimental studies are contained in table 1. The results are recorded in pairs, representing what was done in the 12 eyes of each series of 6 rabbits. The totals for each method of treatment, showing the number of eyes which had completely regenerated on each day, are recorded at the bottom.

10 Friedenwald-Fuqua ointment consists of benzyl benzoate 5 per cent, peanut oil, 37 per cent, wool fat 8 per cent, cetyl alcohol, 10 per cent, glycerin monostearate, 10 per cent, white petrolatum, U S P, 25 per cent.

11 Aquaphor consists of petrolatum, 95 per cent, and cholesterol and its esters, 5 per cent.

12 Buffered sulfanilamide consists of sulfanilamide U S P 75 per cent, calcium carbonate, 10 per cent, urea 9.5 per cent, disodium phosphate, 5 per cent, sodium tetradeccyl sulfate, 0.3 per cent, and chloroazodin, 0.1 per cent.

computation of chi square showed a significant difference between sulfonamide-treated eyes and eyes with simple denudation and between ointment-treated eyes and eyes with simple denudation, it may be concluded, then, that both ointment and powder alone, as well as sulfonamide-containing ointments and powders, deter epithelial regeneration as compared with no therapy at all. On the same day the sulfonamide compounds showed a slightly greater deterring in-

13 In order best to eliminate the factor of chance in these statistics, Dr Harold Austin advised the application of the chi square statistical analysis to these data (Hill, A B. Principles of Medical Statistics, ed 2, London, The Lancet, Ltd., 1939, p 78-96; Peters, C C, and Van Voorhis, W R. Statistical Procedures and Their Mathematical Bases, School of Education, State College, Pa., 1935 pp 404-423). A χ^2 of 0.05 was used in these studies.

fluence on regeneration than did the ointment bases alone, as analyzed by computation of chi square. By the eighth day 100 per cent of the eyes with simple denudation, 50 per cent of the eyes treated with ointment base or with powder base alone and 84 per cent of the sulfonamide-treated eyes had completely regenerated. At this time there was still evidence by computation of chi square that sulfonamide compounds delayed epithelial regeneration. However, on this day it appeared that the ointment base and the powder base delayed healing significantly more than the sulfonamide preparations. By the eleventh day 100 per cent of the sulfonamide-treated eyes were also healed, but the eyes treated with ointments and powder bases were not all healed until the fourteenth day.

There was no significant difference in the incidence of scarring between eyes treated with ointment base or powder base and sulfonamide-treated eyes, although both methods produced more scarring than occurred in the untreated eyes.

Because mechanical denudation involving the limbus has not been a satisfactory experimental lesion in all hands, and because the majority of clinical denudations probably do not involve the limbus, a central lesion 8 mm in diameter, not involving the limbus, was used in another series of animals. The method was as follows:

A sterilized cork borer, 8 mm in diameter, was used to produce the outer border of the lesion. The depth to which the cork borer was allowed to penetrate was controlled by a plunger inserted in the cork borer. Care was taken to produce a central lesion which did not involve the limbus. The circumscribed incision having been made with the cork borer, the cornea was stained. A collodion-soaked swab was then rubbed over the epithelium within the circumscribed area, removing this much epithelium. The cornea was again stained, and spots which were not denuded were then removed by means of a corneal knife, so that an area of even staining of equal diameter and of as nearly the same depth as possible, was obtained in all animals. Ether anesthesia was used.

In this series, 42 animals of the same type as those in the previous series were used. The ointments employed were Vanisol,¹⁴ Aquaphor and hydrous wool fat and petrolatum. The sulfonamide compounds used were 10 per cent sodium sulfadiazine in Vanisol, 10 per cent sodium sulfadiazine in hydrous wool fat-petrolatum ointment and 10 per cent sodium sulfacetamide in Vanisol and in hydrous wool fat-petrolatum ointment.

The results are recorded in table 2. The data on the eyes are not presented here in pairs, as they were in table 1. On the fourth day 55 per cent of the untreated eyes, 43 per cent of the eyes treated with ointment base and 21 per cent of the sulfonamide-treated eyes had regenerated.

¹⁴ Vanisol consists of sodium stearate, 20 per cent cetyl alcohol, 5 per cent, glycerin monostearate, 8 per cent and water 67 per cent.

By the fifth day 94, 97 and 71 per cent respectively had regenerated, by the sixth day, 100, 91 and 92 per cent, and by the seventh day, 100, 100 and 100 per cent. Analysis of these statistics by computation of chi square shows on the fourth day (*a*) no significant difference between the untreated eyes and the eyes treated with ointment base, (*b*) no significant difference between the eyes treated with ointment and the sulfonamide-treated eyes and (*c*) a just significant difference between the sulfonamide-treated eyes and the eyes with no therapy at all. The same method of analysis applied on the fifth and sixth days shows that there is, again, a just significant difference between the sulfonamide-treated eyes and the eyes which received no

TABLE 2.—Influence of Ointments, Powders and Sulfonamide Preparations on Mechanical Denudations Within the Limbus

	Day of Regeneration							Incidence of Scars
	3d	4th	5th	6th	7th	8th	9th	
Simple denudation	2	8	7	1				
Vanisol			2	7	7	2		3
Aquaphor	1	3	2					
Hydrous wool fat-petrolatum ointment, 50% each	2	10	4	2				1
10% sodium sulfacetamide in Vanisol			4	2				
10% sodium sulfacetamide in hydrous wool fat-petrolatum ointment		2	3	0	1			1
10% sodium sulfadiazine in Vanisol	1	2	2	1				1
10% sodium sulfadiazine in hydrous wool fat-petrolatum ointment	1	1	3	1				
Totals								Total Eyes Each Group
Denudation alone	2	8	7	1	0	0	0	18
Ointments alone	3	15	13	9	2	0	0	42
Sulfonamide compounds	1	4	12	5	2	0	0	24

therapy at all, whereas there is no significant difference between the eyes treated with ointment base alone and those treated with sulfonamide compounds.

COMMENT ON EXPERIMENTAL DATA CONCERNING USE OF SULFONAMIDE COMPOUNDS IN OINTMENT AND POWDER VEHICLES

It is evident that the sulfonamide preparations in ointment and powder form have some delaying effect on regeneration of corneal epithelium. This is most striking when the type of lesion used for experimental study involves the limbus and is barely evident when the experimental denudation does not involve the limbus. This observation is of practical importance in that the majority of clinical lesions will proba-

bly be of the central type, in which a barely significant deterring effect is produced on regeneration of corneal epithelium with the use of sulfonamide ointments and powders.

The data show no significant difference in the healing of either type of lesion between the effect of ointment and powder bases and that of sulfonamide-containing ointments and powders. This would indicate that a nonspecific effect of ointments and powders also deters regeneration of corneal epithelium and that the deterring effect noted is not simply a specific effect of the sulfonamide compounds.

To avoid the deterring effect of ointment bases and powders alone, it seemed desirable to determine the influence of the sulfonamide drugs in solutions. The use of a solution would avoid many of the mechanical effects of ointments and powders. However, to maintain adequate levels of the sulfonamide compounds in the cornea with solutions of the drugs, it is necessary to apply the solution frequently.⁹ Higher levels in the aqueous and the cornea are obtained with the

by computation of chi square on the fourth day failed to show a significant difference.

These studies tend to confirm the work of Bellows and Gluckman,⁵ Berens, De Gaia and Loutfallah⁶ and Smelser and Ozanics⁷ in that a sulfonamide compound in ointment or powder form does deter regeneration of corneal epithelium. However, the sulfonamide compounds do not possess this property to a significantly greater extent than do the simple ointment bases and powders used as their vehicles. In the case of lesions which do not involve the limbus, these studies indicate that even the retarding effect of the sulfonamide preparation, as well as that of the ointment and powder base, is just significant and that when a sulfonamide compound in solution is used the retardation is practically nil.

Smelser and Ozanics⁷ suggested that sulfadiazine is more desirable than sulfathiazole or sulfacetamide in that it inhibits cell migration less. The results of the present study indicate no significant difference between the sodium salt of sulfadiazine and that of sulfacetamide in this property. For the same reason, these authors stated the opinion that ointment preparations are better than powders. The present study confirms this conclusion. The data collected here, as well as the investigations of Berens, De Gaia and Loutfallah⁶ and Smelser and Ozanics⁷ indicate that some mechanical factor contributed by the vehicle must be considered and that the chemotherapeutic agent itself is not solely responsible for the retarded regeneration of corneal epithelium when it occurs.

If the influence of the ointment bases alone is considered and the data of table 2 are further analyzed, one finds that Vanisol is significantly more harmful than hydrous wool fat-petrolatum ointment. The 6 eyes treated with Aquaphor are too few to allow statistical evaluation of the effect of this vehicle, but it seems to lie between hydrous wool fat-petrolatum ointment and Vanisol in its retarding action. Smelser and Ozanics⁷ found hydrous wool fat to be somewhat less irritating than Aquaphor in rat eyes. Recent studies by Bellows¹⁵ disclosed that the vanishing type of ointment, similar to the Vanisol used here, was a very irritating ointment.

It seems evident from these data that there is little risk of retarding epithelial regeneration in using sulfonamide compounds in ointments, particularly in hydrous wool fat and petrolatum, to prevent secondary infection in epithelial denudations of the cornea which do not involve the limbus. The risk becomes greater when the

15. Bellows, J. G. Penicillin Therapy in Ocular Infections, Am. J. Ophth. 27:1206 (Nov.) 1944.

TABLE 3.—Influence of 10% Sodium Sulfadiazine on Regeneration of Corneal Epithelium

	Day of Regeneration				Total No. of Eyes
	3d	4th	5th	6th	
Isotonic solution of sodium chloride	4	5	1		10
10% sodium sulfadiazine in isotonic solution of sodium chloride	2	6	1	1	10

sodium salts than with the acid preparations of the sulfonamide compounds.⁹ For these reasons, 4 drops of 10 per cent sodium sulfadiazine in isotonic solution of sodium chloride was applied to the right eyes of 10 rabbits at 8:30 a.m., 10 a.m., 11:30 a.m., 1 p.m., 3 p.m., 5 p.m., 7 p.m., 9 p.m., 11 p.m. and 12:30 a.m. of each day. The left eyes served as controls and received 4 drops of isotonic solution of sodium chloride alone at the same time intervals. The pH of the solution of sodium sulfadiazine was approximately 10. The corneas were denuded by the method described by Bellows and Gluckman, tetracaine being used instead of cocaine for local anesthesia. The eyes were stained with fluorescein each day, as in the previous series, and the results are included in table 3.

These results indicate that sodium sulfadiazine did not retard significantly the regeneration of corneal epithelium as compared with isotonic solution of sodium chloride even though the denudations included the limbus. On the fourth day 90 per cent of the eyes treated with isotonic solution of sodium chloride and 80 per cent of the sulfonamide-treated eyes had regenerated. Analysis

denudations involve the limbus. With the employment of solutions the task is slight regardless of the extent of the denudation.

CONCLUSIONS

The influence of locally applied sulfonamide compounds in ointment and powder form on regeneration of corneal epithelium varies, depending on whether the lesion does or does not involve the limbus.

Ointment bases and powder bases alone and sulfonamide-containing ointments and powders deter regeneration of corneal epithelium to a greater degree in denudations involving the limbus than in denudations within the limbus.

Little significant difference was found between the effect of the ointment bases and powder bases alone and the sulfonamide-containing ointments and powders on the rate of regeneration of corneal epithelium.

A 10 per cent solution of sodium sulfadiazine had little or no deterring effect even on denudations involving the limbus. It is evident, therefore, that the major deterring action of sulfonamide compounds on regeneration of corneal epithelium must be due to some mechanical effect of the vehicle. We cannot speculate as to what this factor is on the basis of this study.

Scarring of the cornea was more frequent in the treated denudations than in the untreated ones, but there was no difference in the incidence of scarring between the eyes treated with sulfonamide ointments and powders and those treated with ointments and powders alone.

Smith, Kline and French Laboratories supplied the microcrystalline sulfadiazine, Wallace and Tiernan Products, Inc., the buffered sulfanilamide, and the Schering Corporation, the sodium sulfacetamide.

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CHOROIDEREMIA

REPORT OF A CASE

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Choroideremia has been defined as a condition in which the choroid and the pigment layer of the retina eventually disappear. The disease is bilateral, the periphery of the fundus becoming involved early in the process and the macula late. Thus, the first symptoms are usually night blindness and loss in the field of vision.

The condition was first described by Mauthner in 1871, and 28 cases have been reported in the literature to date. The following case is that of a patient first seen at the eye clinic, Queens General Hospital, on May 19, 1944.

REPORT OF CASE

History—W W, a white man aged 58, complained that he could not see at night and that because of this he always had to be home before dark. He had been employed as a janitor for fifteen years. About ten years ago, at which time he was working only at night, he began to notice that he had difficulty in seeing at night. This difficulty became progressively worse, so that three years prior to consultation he asked to be transferred to day work.

Past History—About 1924 he had difficulty with his eyes. His memory is not very clear about this episode, but he recalled that his vision was blurred and that he suffered from photophobia. At that time he was admitted to the Brooklyn Eye and Ear Hospital, where he was treated with drops. As a result of roentgenographic examination, all his teeth were extracted. He made a complete recovery. (I wrote for a report, but no records of his case were available.)

Family History—His father died at the age of 70. He had worked as a night watchman until two years before he died. His mother died when she was 69. Her vision was good. Three brothers and one sister are dead, and there are two living sisters, none of whom had ever had symptoms of night blindness. There were four living children. The oldest was 33 and was in the Army of the United States overseas. The other children were 14 years, 3 years and 19 months of age. Examination, with the use of a mydriatic, revealed that the fundi were normal. There was no history of consanguinity of the parents or of the grandparents.

There was no evidence of a functional disorder.

From the service of Dr Guernsey Frev, Department of Ophthalmology, Queens General Hospital, Jamaica, N Y

Physical Examination—The patient was well developed and physically and mentally active. His blood pressure was 154 systolic and 86 diastolic. The only abnormality was cloudiness of the left antrum and the right ethmoid cells, as noted in roentgenograms.

Laboratory Report—The Wassermann reaction was negative. The blood sugar measured 95 mg per hundred cubic centimeters. Urinalysis revealed nothing abnormal. The blood cell count, including the differential count, was normal.

Examination of the Eyes—Visual Acuity Vision was 20/70 in each eye without correction. It was 20/20 in the right eye with a correction of —1.75 D cyl, axis 85 and 20/30 in the left eye with a correction of —0.50 D sph —1.00 D cyl, axis 95.

External Examination—The lids of both eyes were normal. The conjunctivas were clear. The corneas were clear except for arcus senilis. The anterior chambers were clear. The irises were of normal appearance. The pupils were equal and regular and reacted well in accommodation but responded sluggishly to light. The lenses were normal.

Study of the Fundi—Examination of the right fundus revealed a peculiar greenish white reflex except at the disk, the macula and the extreme periphery of the fundus. The margins of the disks were slightly indistinct, but the disk markings were normal, with no signs of atrophy. The blood vessels were generally attenuated, branched normally and showed no signs of sclerotic changes.

In the macular area there was a collection of pigment, of about $\frac{1}{4}$ disk diameter, which rested on a background giving a pink reflex, of about 1 disk diameter.

Except for the macular area and the extreme periphery, the choroid appeared to be completely absent. The blood vessels stood out sharply against the greenish white background, and in the macular area they appeared to be in two layers—one superficial and the other deep. Scattered throughout the fundus were a few small collections of pigment. These did not have the appearance of the pigment seen in cases of retinitis pigmentosa.

In the extreme periphery choroidal vessels and pigment were seen. This area formed a complete ring but seemed slightly wider temporally.

The left fundus showed essentially the same picture as the right.

Slit Lamp Examination—No changes were noted in the anterior segment of the eye. A careful study of the anterior portion of the vitreous failed to show collections of pigment, as noted by one observer (Scobee¹).

¹ Scobee, R G. Choroideremia, Am J Ophth 26: 1135-1143 (Nov) 1943

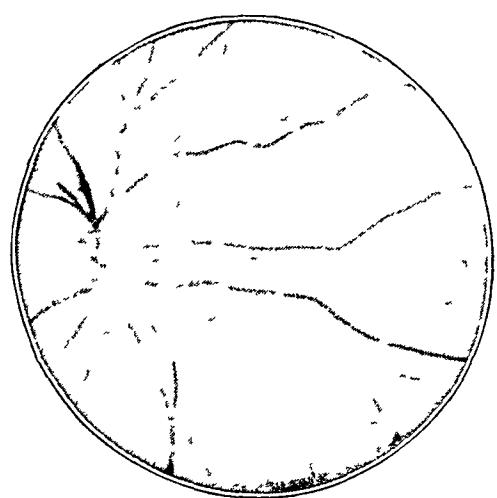


Fig 1—Photograph showing the disk and the nasal retina of the right eye

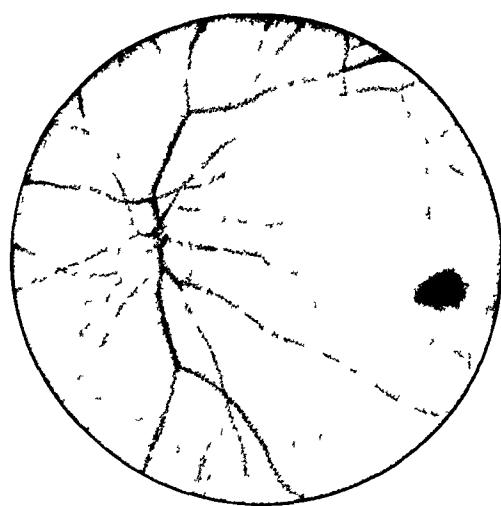


Fig 2—Photograph showing the disk and the macular area of the left eye

Study of the Visual Fields There was a central visual area of from 5 to 10 degrees about the fixation point of each eye. With a 17 mm white test object at 330 mm a narrow peripheral field was obtained, which formed a complete ring except for the upper part of the field. The fields were almost identical in the two eyes (fig. 4)

COMMENT

In her textbook "Developmental Abnormalities of the Eye," Mann² suggested that choroideremia is caused either by (a) failure of the

owing to its rarity, the failure to observe cases early and the absence of material for microscopic examination

In 1937, Bedell³ made a complete review of the literature and, in addition, reported several cases that he had observed personally. He stated the belief that the condition is a postnatal pathologic dissolution of the choroid. Other cases have been reported by Friedman (1940),⁴ Shapira and Sitney (1943)⁵ and Scobee (1943).¹

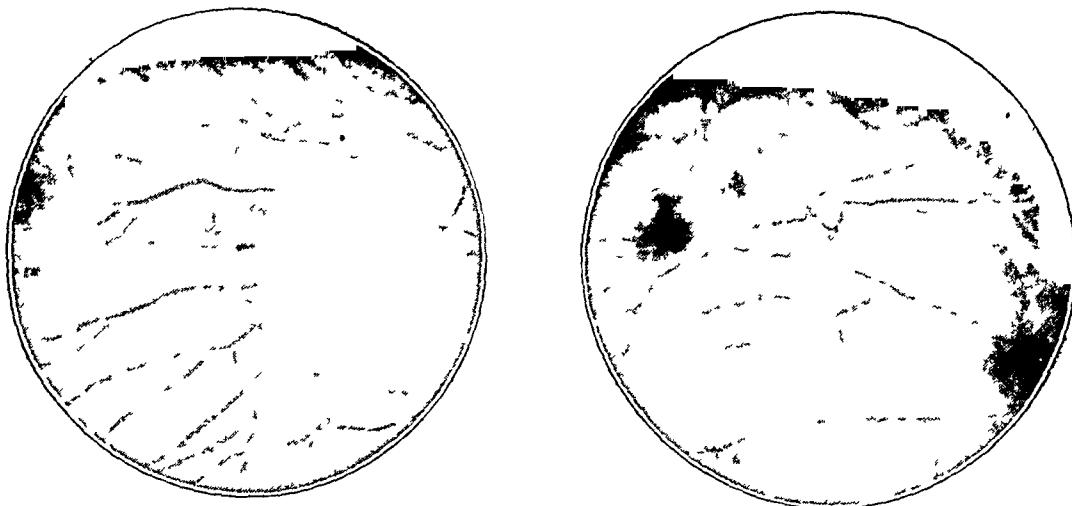


Fig. 3.—Photographs showing the periphery of the fundus, with pigment, of the right (A) and of the left (B) eye.

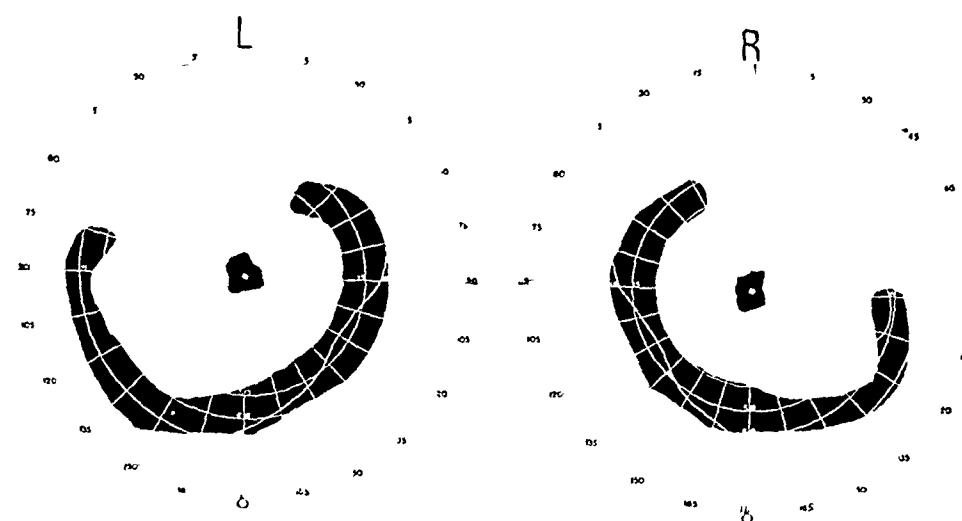


Fig. 4.—Visual fields obtained with a 17 mm white test object at 330 mm. In the left eye vision was corrected from 20/70 to 20/30 and in the right, from 20/70 to 20/20.

ciliary arteries to bud at the 16 mm stage or by (b) failure of the outer layer of the optic cup to produce pigment (at the 10 mm stage), with the result that the stimulus for the capillary growth may fail, even though the arteries do bud. She expressed the opinion that choroideremia is a developmental condition but admitted that its origin is not fully understood,

Scobee reported 2 cases, in brothers. He was able to follow his patients and show by examinations of the fundus and studies of the visual fields definite progress of the pathologic condition over a relatively short time. His observa-

³ Bedell, A. J. Choroideremia, Arch Ophth 17:444-467 (March) 1937

⁴ Friedman, B. Choroideremia, Arch Ophth 23:1285-1287 (June) 1940

⁵ Shapira, T. M., and Sitney, J. A. Choroideremia, Am J Ophth 26:182-183 (Feb.) 1943

² Mann, I. Developmental Abnormalities of the Eye. New York, The Macmillan Company, 1937

tions and those in the case reported here tend to confirm the opinion that the pathologic process is postnatal rather than congenital.

Verhoeff⁶ expressed the opinion that many cases of supposed choroïderemia are actually instances of retinitis pigmentosa in which the choroid is hidden by widespread gliosis of the degenerated neuroepithelium. The many persons who observed the case reported here stated the belief that it was a case of true choroïderemia, and not one of gliosis.

SUMMARY

A case of choroïderemia was observed in a man 58 years old. The patient had only slight myopia, whereas most of the patients reported on

with this condition have shown a moderate or a high degree of myopia. The disease progressed over a period of ten years, so that a change from night to day work was necessary three years ago. The fundus and the defects of the visual fields were practically identical in the two eyes. Acuity in the central visual fields remained excellent despite the advanced stage of the disease.

Photographs of the fundus were made by Marfan of the Institute of Ophthalmology, Presbyterian Hospital, New York.

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⁶ Verhoeff, F. H. Retinitis Pigmentosa with Widespread Gliosis—So-Called Choroïderemia, *Arch Ophth* **27** 688-691 (April) 1942.

PARINAUD'S OCULOGLANDULAR SYNDROME DUE TO A YEASTLIKE ORGANISM

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At the present time it is well established that what was first known as Parinaud's conjunctivitis after its description by that author in 1889, is not a definite disease with specific pathologic and bacteriologic characteristics, but is in reality a symptom complex which can be caused by a number of etiologic factors. For that reason the term "Parinaud's oculoglandular syndrome,"¹ for a chronic unicocular granulomatous conjunctivitis with regional lymphadenitis, appears most appropriate. Tularemia, tuberculosis, an unidentified virus infection, lymphogranuloma venereum, syphilis and even infections with the hemolytic staphylococcus and *Bacillus proteus*,² have been listed as causes of the condition. But by far the most common agent appears to be the leptothrix first found in pathologic sections by Verhoeff, in 1913 and later obtained in cultures of conjunctival material by Verhoeff and King, in 1933.³ Others have confirmed these observations and have also demonstrated the organism in the preauricular gland.⁴

While in still other cases of the syndrome no etiologic agent has been discovered, it is likely, as Duke-Elder,⁵ stated, that as more cases are studied still other causes will be brought to light.

It is the purpose of this paper to report another case of Parinaud's oculoglandular syndrome in which the condition was rather severe and appears to have been due to infection with an

1 Duke-Elder, W S Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1938, vol 2, p 1629

2 Zuccoli, A Ueber Proteus-Conjunctivitis zugleich ein Beitrag zur Kenntnis des sogenannten Parinaudschen Syndroms, Schweiz med Wchnschr 18 803 (Aug 21) 1937

3 Verhoeff, F H Parinaud's Conjunctivitis A Mycotic Disease Due to a Hitherto Undescribed Filamentous Organism, Arch Ophth 42 345, 1913

4 Verhoeff, F H, and King, M J Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis) Artificial Cultivation of the Leptotriches in Three of Four Cases, Arch Ophth 9 701 (May) 1933

5 Wright, R E Isolation of Verhoeff's Leptothrix in a Case of Parinaud's Syndrome Arch Ophth 18 233 (Aug) 1937

6 Duke-Elder¹ p 1630

unidentified yeastlike body, and to suggest an additional cause for the condition.

REPORT OF A CASE

Lieut C T, aged 30, was first seen at the eye clinic of the Miami Beach Training Base on June 24, 1943. About ten days previously his right eye had become inflamed, and a few days later the right preauricular gland had begun to enlarge. His past history was essentially noncontributory.

Examination of the right eye at this time revealed the vision to be 20/20. There were considerable edema and pseudoptosis of the right upper lid, due to severe conjunctivitis, which involved only the upper lid and the fornix. On the injected and edematous conjunctiva were a number of rounded, raised, yellowish gray nodules, varying in diameter from 0.5 to 4 mm. These were mainly situated at the upper tarsal border. Although superficial, they were not ulcerated. The eye itself, as well as the conjunctiva of the lower lid, was normal and remained so during the entire course of the disease. The right preauricular gland was swollen and tender.

The left eye was entirely normal in all respects.

General physical examination revealed nothing abnormal.

The diagnosis of Parinaud's oculoglandular syndrome was made, and investigations as to the exact cause were begun. The results of laboratory examinations are noted later.

The condition progressed, and in the course of a week the conjunctival nodules increased in both size and number. The preauricular gland increased to the size of a plum, and two almond-sized nodules appeared on the right side of the neck. The patient was admitted to unit 1 of the station hospital on July 3, and the largest nodule was removed for biopsy. Several smaller nodules were taken on July 7.

For the first five days after his admission the patient was rather ill, his temperature rose to 101.4 F, and he complained of considerable pain in the enlarged glands. Thereafter he was entirely afebrile.

On his admission administration of sulfadiazine was begun, but was discontinued after several days because of nausea. In place potassium iodide was given, but use of this drug, too, had to be stopped because of the development of a pustular eruption.

By July 14 the conjunctival infiltrates had disappeared and the eye had assumed a normal appearance. The glands, however, continued to be painful, swollen and tender. Roentgen therapy was instituted and resulted in softening and suppuration. The preauricular gland was drained surgically on July 24, and about 15 cc of pus was obtained. Bacteriologic studies of

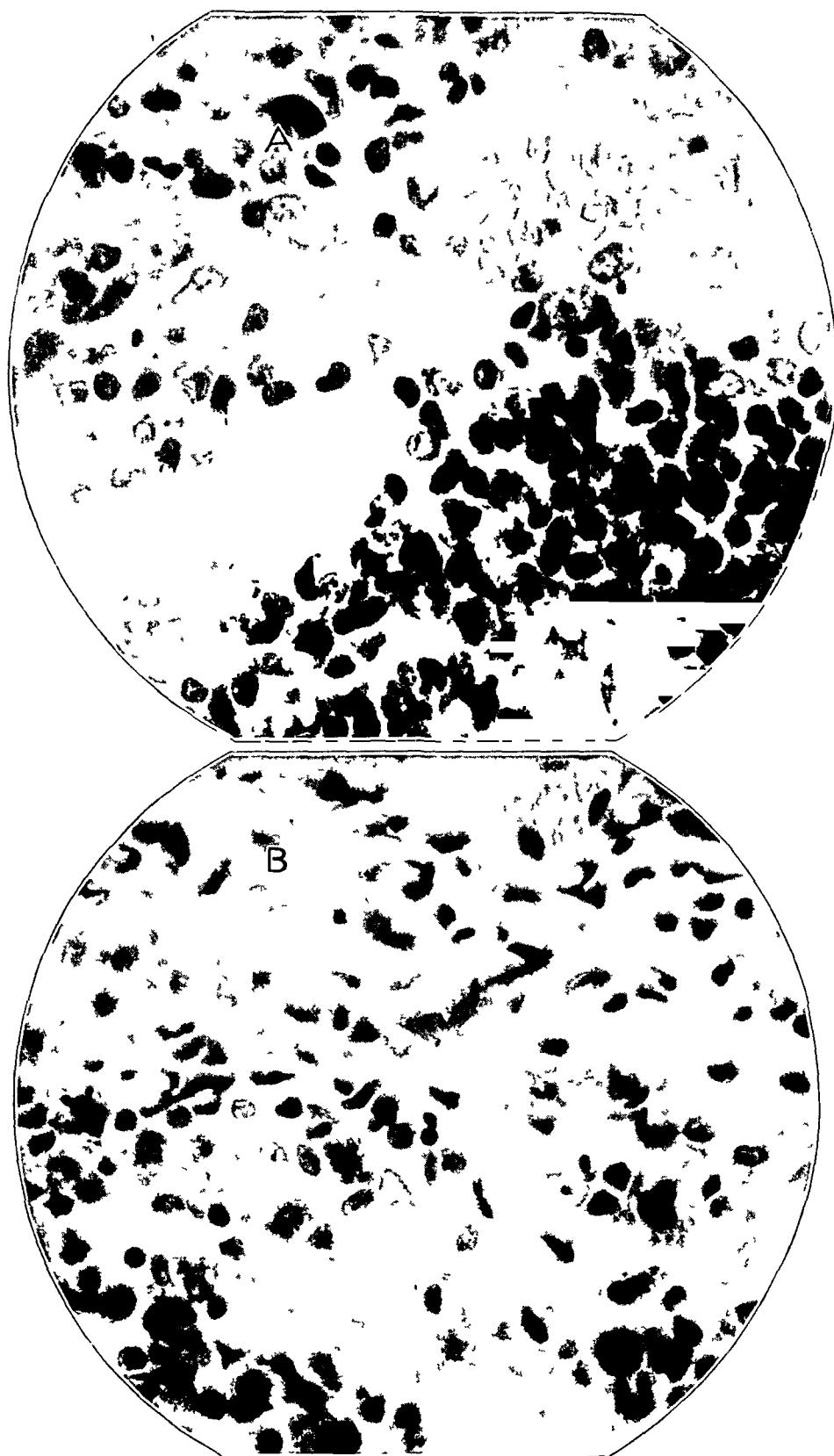


Fig 1.—Photomicrographs of biopsy specimens from the conjunctiva, showing (A) scattered yeastlike bodies, and (B) a number of yeastlike bodies. In the center (B) one of these bodies, having an hourglass shape, appears to be budding. Magnification, 2,175.

the pus, reported later, gave significant results. On August 19 the larger of the two glands in the neck was incised and from this also pus was obtained. It required two months for the first incision to heal, thereafter the area involved remained indurated, and the tissue reaction in general suggested an unusual type of infection. Nine months after the incision of the cervical gland the wound in the neck was still draining to a slight extent.

Laboratory Examinations—Smears, epithelial scrapings and cultures of secretions from the conjunctiva, with the use of special mediums, were all negative for pathogens. However, examination of the material obtained from the conjunctiva revealed a yeastlike body. A similar yeastlike body was found in the pus from the preauricular gland. This was considered the etiologic agent.

The biopsy specimens, both the material fixed in formaldehyde and that fixed in Zenker's solution, were variously prepared with hematoxylin and eosin, Giemsa's stain, the Ziehl-Neelsen method and the Verhoeff modification⁷ of the Gram stain, which was used to demonstrate the leptothrix. The best results were obtained with hematoxylin and eosin and the Verhoeff stain. The sections showed that the conjunctival nodule was composed essentially of granulation tissue, with masses of lymphocytes, plasma cells and many fibroblasts in various stages of development, as well as new-formed blood vessels. The nodule was ulcerated at the surface, the surrounding tissue showed evidence of necrobiosis (poor staining, pyknosis and distortion of cells). A number of polymorphonuclear leukocytes occurred in this region but were not found to any extent deeper in the section. Numerous phagocytes containing granules taking a deep blue stain were noted. Rare giant cells were seen. Throughout the section, especially in the more superficial portion, round or oval objects, slightly larger than an erythrocyte, lay scattered about. These objects took a uniform deep blue, almost black, stain, with no central paler portion (fig 1A). Some of them seemed to have a single or double refractile ring, or halo, about them. A number appeared to be budding. Several had an hourglass shape (fig 1B), while others seemed to have small satellites around them. The objects just described appeared quite different from the lymphocytes present, in the more necrotic zone they retained their characteristics to a much greater extent than the cellular elements and thus stood out readily. It was felt that these objects fulfilled most of the morphologic requirements of yeasts and beyond doubt could be considered as such. No leptotriches were found.

Bacteriologic examination of the pus obtained from the preauricular gland revealed similar yeastlike bodies on direct smears stained with the Gram method (fig 2A and B). On culture an unidentified yeast was grown but, unfortunately, was discarded, as it was erroneously thought to be a contaminant. Studies of the pus obtained from the cervical gland showed no organisms of any kind.

The slides were reviewed by Lieut Col Phillips Thigerson. He saw the bodies described and felt that they were probably the causative agent. He advised, however, inasmuch as positive cultural evidence was

⁷ Verhoeff, F H. Improved Method of Staining Within Tissues Leptotriches of Parinaud's Conjunctivitis and Gram-Positive Micro-Organisms, J A M A 115 1546 (Nov 2) 1940

lacking, that the case be reported as one in which the condition was due to a yeastlike organism. He, too, found no leptotriches. This opinion was later concurred in by Major James H Allen. Dr Alson E Braley⁸ also thought that the bodies could be yeasts.

The usual laboratory tests, such as the blood count, urinalysis and Kahn test of the blood, gave normal results. Agglutination tests for tularemia gave negative results on three occasions, as did tests for undulant fever and heterophile antibodies. The Frei and Mautoux tests likewise gave negative results.

COMMENT

In the case of Parinaud's oculoglandular syndrome described here a yeastlike body was found both in biopsy specimens from the conjunctiva and in smears of pus aspirated from the preauricular gland. It is believed that an unidentified yeastlike organism was the cause of the condition. This opinion was concurred in by several authorities in the field of ophthalmic bacteriology.

There can be little doubt that the case falls into the broad group of conditions known as Parinaud's oculoglandular syndrome. The conjunctival lesions, the glandular involvement, the clinical course, the prompt cure of the conjunctivitis after excision of the involved portions, all follow the usual description of this syndrome. The only unusual feature is the glandular suppuration and induration, with extremely slow healing. This points to an unusual etiologic factor and is entirely consistent with the characteristics of a yeast infection.

Glandular suppuration is rare in cases of Parinaud's oculoglandular syndrome. Verhoeff⁹ did not observe it in his cases of the syndrome due to the leptothrix. McKee,¹⁰ in emphasizing the rarity of suppurative glands, mentioned 2 exceptions, notably 1 of Parinaud's original cases, reported in 1889, and cases reported by Gifford, in 1898, in which suppuration was frequent. These early cases were not as completely studied as later ones and not much can be stated about the etiologic factors. It appears, therefore, that glandular suppuration is not present in the type of Parinaud's oculoglandular syndrome designated by Verhoeff as "leptotrichosis conjunctivae," while in other types it may occur.

⁸ Dr Braley and Mr A Marsang, of the Institute of Ophthalmology, Presbyterian Hospital, New York, made the photomicrographs.

⁹ Verhoeff, F H. Observations on Parinaud's Conjunctivitis (Leptotrichosis Conjunctivae), Am J Ophth 1 705 (Oct) 1918

¹⁰ McKee, S H. Parinaud's Conjunctivitis with Suppuration in the Pre-Auricular, Sub-Maxillary and Supra-Clavicular Glands, Tr Am Ophth Soc 25 236, 1927

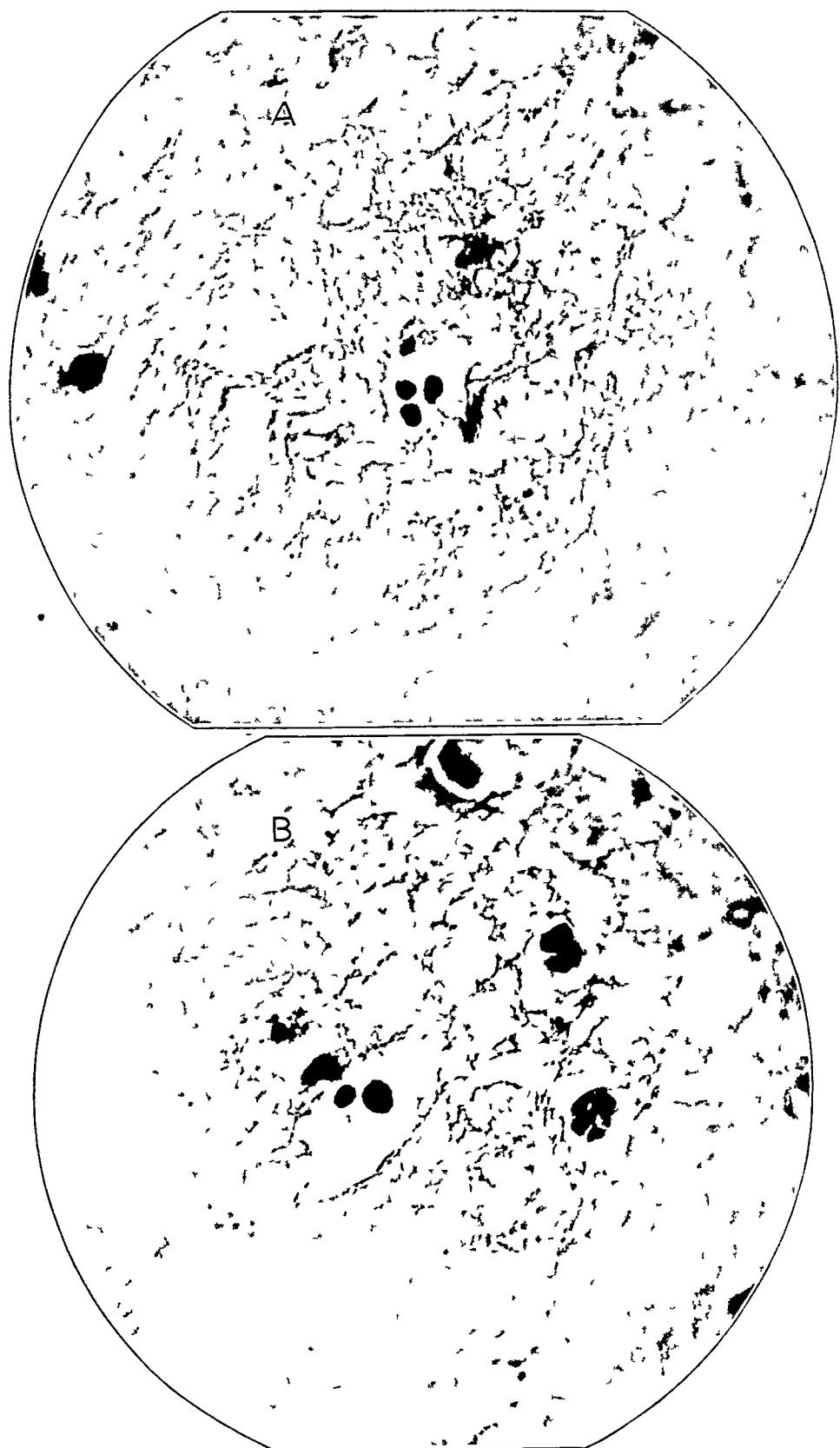


Fig 2.—Gram stain of pus from the preauricular gland, showing (A) group of three yeastlike bodies and (B) other yeastlike bodies Magnification, 2,175

In the case described in this paper the lepto-thrix was carefully searched for, without success, by all who studied the slides. Furthermore, the histologic picture did not conform to that present in the cases in which the condition was due to the lepto-thrix.

In conclusion, in my opinion Duke-Elder's concept that Parinaud's oculoglandular syndrome is a complex of symptoms that may result from infection with any one of a number of known or unknown agents is the most tenable one, in the light of present knowledge. It is thought that in this paper a new cause has been demonstrated, an organism resembling a yeast, which, unfortunately, could not be further classified.

SUMMARY

The case of Parinaud's oculoglandular syndrome reported here was unique in that, while the ocular condition cleared in a few weeks, regional glandular suppuration occurred, requiring surgical drainage, and ultimate healing was prolonged. Both biopsy material from the involved conjunctiva and smears of pus aspirated from the preauricular gland revealed an organism resembling a yeast. In view of the clinical course and the laboratory findings, it is believed that this yeastlike organism was responsible for the disease.

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MANAGEMENT OF PARALYSIS OF DIVERGENCE

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A number of papers have been written on the etiology,¹ physiology and pathology of paralysis of divergence, and various treatments have been devised therefore, there is no need to go into these phases of the subject now.

Divergence and its antagonist, convergence, are essential in the maintenance of fusion. By divergence^{1b} is meant the ability of the visual axis of both eyes when converged on near objects to separate in order to sight on an object more remote.

The findings in cases of paralysis of divergence are as follows:²

1 There is diplopia in the midplane for distant vision.

2 The diplopia is equal in all directions of gaze at the same distance from the subject's eyes.

3 The diplopia is eliminated as the eyes converge to near distances, varying from 2 to 10 feet (60 cm to 3 meters), and then binocular vision is obtained.

4 The images are homonymous and separate farther as the test object is farther withdrawn from the subject.

Many etiologic factors have been suggested, and they are as varied as the number is great. There are several conditions from which paralysis of divergence must be differentiated and which have been adequately discussed before, therefore, they need not be considered here. The purpose of this paper is to report 2 cases in which operation was performed by the late Dr. Sanford R. Gifford. However, there were others in which use of small amounts of prism made operation unnecessary and therefore which are not reported here. Bruce^{1b} stated that resection or advancement of one or both rectus muscles is the logical procedure. Stokes^{1a} mentioned the operations described by Theobald in 1886, by Uthoff in 1893 and by Sachs in 1898. These operations were

tenotomy of one internal rectus muscle, tenotomy of both internal rectus muscles and advancement of the external rectus muscle. Stokes stated that it would seem more rational to perform an advancement or a resection of both external rectus muscles in cases in which the paralysis is stationary.

Gifford felt that shortening of one or both external rectus muscles by the O'Connor cinch method was the safest surgical procedure because if an overcorrection is obtained one or more cinch sutures can be removed as soon as the overcorrection is noted. On the other hand, if an insufficient amount of paralysis has been corrected, the residual divergence can be corrected by use of the same technic on the external rectus muscle of the fellow eye. I have been unable to find any mention of the use of the O'Connor cinch operation for correction of this condition, although the operation is employed in many parts of the country for various other muscular anomalies.

REPORTS OF CASES

CASE 1—J. M., a medical student aged 22, was seen in the eye clinic on Feb. 19, 1941, complaining of diplopia for distance, first noticed about two years previous to this date. This difficulty had become increasingly worse until the time of his first examination. He also complained of a dull headache at this time.

Examination revealed mild folliculosis of the conjunctiva of the lower lid. The cornea, sclera, iris, anterior chamber, lens and pupillary reflexes were normal. With a correction of + 0.25 D sph, axis 90° for each eye vision was 20/13. In the cover test a 10 D prism base out for distance, at 20 feet (6 meters), and a 4 D prism base out for near vision were necessary to overcome the diplopia.

He was seen again on March 8, 1941, and examination showed that the diplopia increased as greater distance was obtained between the observer and the test object and was equal in all fields of vision. The diagnosis of paralysis of divergence was made, and an O'Connor cinch operation on one or both external rectus muscles was advised. An eight strand cinch suture operation was performed on the left external rectus muscle on June 13, 1941, at Passavant Hospital. The sutures were removed on June 26, at which time his eyes were straight for near and distant vision. The diplopia was relieved, but he still complained of frontal headache, which was not affected by reading and which came on shortly after arising in the morning. He was followed in the clinic at intervals until his graduation from medical school and was last seen on Dec. 16,

From the Department of Ophthalmology, Northwestern University Medical School.

1 (a) Stokes, W. H. Paralysis of Divergence, Arch. Ophth. 11: 651-664 (April) 1934. (b) Bruce, G. M. Ocular Divergence. Its Physiology and Pathology, ibid. 13: 639-660 (April) 1935.

2 Gifford, S. R. Textbook of Ophthalmology, Philadelphia, W. B. Saunders Company, 1941. Stokes^{1a}

1943, at which time he had no recurrence of diplopia. He still had headaches, not related to the use of his eyes, and his measurements with Maddox rods were 3 prism diopters of esophoria for distance, 1 prism diopter of esophoria for near vision and no vertical deviation.

CASE 2—Mr C G, aged 34, was seen by Dr Sanford Gifford on Nov 11, 1943, complaining of diplopia for distance, dating back as far as he could remember. The degree of diplopia was constant. He was wearing a correction of -0.50 D sph with a 4.5 D prism base out for the right eye (vision 20/15) and -0.50 D sph with a 5.5 D prism base out for the left eye (vision 20/20). The lids, conjunctiva, cornea, sclera, iris, anterior chamber, lens and fundus were normal. In the cover test he had esophoria for near and for distant vision. Without his glasses the diplopia was corrected by a 13 D prism base out for distance. He had diplopia beyond 11 inches (33 cm) but none closer. His near point of convergence was 3 minutes. The diplopia increased as the test light was drawn farther away from the subject and was equal in all directions. The Maddox rod showed 12 prism diopters base out for distance and no lateral deviation for near vision. A diagnosis of paralysis of divergence was made, and an O'Connor cinch operation on the left external rectus muscle was advised.

The patient was admitted to Passavant Hospital and an eight strand cinch suture operation was performed on the left external rectus muscle on Jan 8, 1944. He was seen again on Jan 27, 1944, and the cover test showed that his eyes were straight for both near and distant vision. He was able to converge to 8 inches, and the Maddox rod test revealed 6 prism diopters of exophoria for distance and 4 prism diopters of esophoria for near vision. The diplopia was entirely relieved,

and the cinch sutures were removed. He has been free from symptoms and has had no complaints since the operative procedure.

MANAGEMENT OF PARALYSIS OF DIVERGENCE

Dr Gifford managed cases of paralysis of divergence in the following way:

1 Patients needing a small amount of prism base out to superimpose images at distance were given correction for distance, or simple prism lenses base out were prescribed if no correction for distance was needed.

2 Patients needing a larger amount of prism base out for correction of diplopia at distance were advised to have an O'Connor cinch operation on one or both external rectus muscles, depending on the amount of prism necessary to superimpose the images at distance. It is estimated that each strand of the cinch suture will correct approximately 1½ prism diopters of deviation when the operation is performed on the lateral rectus muscle with nothing done to the opposing muscles.

The views expressed in this paper concerning the type of operation to be performed in cases of paralysis of divergence are those of the late Dr Sanford R Gifford, at whose suggestion I wrote this report.

Northwestern University Medical School

VISUAL EXERCISES IN OPHTHALMOLOGY

JOSEPH I PASCAL, MD
NEW YORK

The subject matter of this paper pertains to work which, I think, will form a larger portion of ophthalmologic practice in the future than it does at present. I am using the term visual exercises in its widest possible application.

All are familiar with exercises which are used to develop and improve central macular vision. I think it is generally agreed that these exercises do not increase macular acuity in the physiologic sense. The improvement in vision which results in a great many cases is most likely due to an intensification of the psychic phase of the act of seeing. As Dr Lancaster¹ has so aptly put it in a recent article, "seeing is only half ocular—the other half is cerebral."

The improvement of central vision is often a large part of the orthoptic treatment of squint. The dulled central vision of the deviating eye is called amblyopia ex anopsia which term immediately suggests that the cause of the poor vision lies in failure to use the eye. It is the mind which fails to function for the amblyopic eye has been open all the time and has received the same retinal images as the other eye. The remedy of course is to force the patient to apply his mind to the images in the deviating eye and to use this eye as far as possible for critical, detail vision.

There are numerous ways of exercising the amblyopic eye, and every practitioner usually adds some of his own design. The mental aspect is all important, and these exercises as far as possible must be interesting to the patient. They must create a pleasurable mental tone, such an exercise is watching an interesting moving picture with the amblyopic eye.

In general, there are two or three principles which govern the multitudinous exercises of this type. One is to introduce into the exercises a good deal of motion, making the seeing process dynamic. This is accomplished, for example by watching a rotating target or a swinging light. Another is to introduce a variety of colored

Presented before the New York Society for Clinical Ophthalmology, Jan 8, 1945

¹ Lancaster, W B Present Status of Eye Exercises for Improvement of Visual Function, Arch Ophth 32 167 (Sept) 1944

patterns, such as the old-fashioned kaleidoscope provided. Still another is to associate the act of seeing with some activity of the body, some motor expression, usually of the hands. But other exercises, such as motor activities of the organs of speech or a motor reaction of the legs, may be included. Still other examples are stringing colored beads or sticking colored pins into selected letters, as a sort of game.

Now what has happened in cases of amblyopia when, for example, initial vision with the best correction is 20/100 and after a period of exercises the vision improves to 20/30 or 20/20? The retinal images of the letters on the 20 foot (6 meter) line at the end of the training period are not focused any better than they were at the beginning, nor are they different in size, shape or form. Why are they legible now when before they merely registered as indistinct blotches? The answer is simply that the mind has been trained to interpret the former retinal "blotch." The improvement in vision is due entirely to a better response in the psychologic phase of seeing.

This is indeed a remarkable phenomenon, but no stranger than what one frequently encounters in everyday life. A smudge on the horizon over the sea which to the landlubber may be a cloud, or what not, is at once recognized by the experienced seaman as a vessel. The retinal images in the eyes of the two observers may be exactly the same in clarity, size and shape, but the mental contribution to this retinal image is vastly different. With visual exercises better use of the amblyopic eye has been accomplished for the letters or figures on the Snellen chart and, by extension, for all familiar objects.

From these considerations the thought irresistibly forces itself on the mind. Why cannot this process be extended? If the psychic contribution to vision can be so greatly enlarged in these cases after the correction of the ametropia, why can it not be developed, to some extent at least, without the correction of the ametropia? To be sure in the uncorrected amblyopias one is dealing with a nonfocused retinal image, as against a focused retinal image in the corrected amblyopias.

But the mind registered the focused retinal image only as an indistinct retinal blotch before it was trained to respond to this blotch in terms of definite form perception. Why cannot the mind be trained to respond likewise to an unfocused retinal blotch? The response to such an image may not be so pronounced, but there seems to be no reason that significant improvement cannot be developed. The fact is that this can be done and has been done.

I know that in saying this I am treading on unorthodox territory, and it is true that this field has been exploited perhaps overexploited by some licensed and unlicensed practitioners. But this does not vitiate whatever is sound in the procedure.

When Huxley's book "The Art of Seeing"² came out, the author and his book were severely criticized by leading authorities in ophthalmology. It was therefore with a good deal of temerity that I ventured to write in defense of the author and the system loosely called the Bates system.³ One can imagine my relief on seeing the article on this subject by Dr Lancaster in the ARCHIVES. This article should be read and reread until one becomes thoroughly familiar with this broad viewpoint toward visual exercises.

Not only central vision but peripheral vision can be improved with training and exercise. Dr Frank M Low, of the School of Medicine of the University of North Carolina, has done some interesting work along this line. He has shown that peripheral visual acuity is independent of central acuity and, like the latter, can be improved with training. Exercises to improve peripheral vision may not be necessary for the average person. But improved peripheral vision is certainly a great help in many lines of endeavor, aside from aviation. Many a poor or accident-prone driver may owe his difficulties to inefficient peripheral vision. And many a worker in an industrial plant may have a greater margin of safety from accidents by developing more efficient peripheral vision. Incidentally, the fact that peripheral vision improves with training may have a bearing on testing of the visual fields when such tests are made repeatedly, as in cases of glaucoma and other conditions.

There has been quite a stir recently regarding claims for the cure of color blindness by means of visual exercises. The reports have aroused a

good deal of controversy, some rather acrimonious. The facts as far as they were ascertained, however, did show that a number of men who were rejected by the Army, Navy and Air Forces because of color blindness passed the required tests after the training. The conservative view of this process taken by *The Journal of the American Medical Association* was that the exercises did not "cure" the color blindness, but merely "educated" the candidate or trained him in some way for better color perception.

Probably the use of the word "cure" is not appropriate in the claims for treatments which tend to improve color discrimination. Although it may be quibbling about terms, one may ask whether one really "cures" disease or whether one merely provides favorable conditions for the inherent recuperative powers of the body and mind to assert themselves? However, whether these men were "cured" or "educated," they could distinguish the colored patterns on the Ishihara or similar plates after a series of exercises, something which they could not do before the training. And the skill to distinguish the colored patterns on the plates certainly was carried over to other objects and colored configurations. It is no exaggeration to say that these persons have acquired a greater degree of color perception and color discrimination than they had before taking the exercises.

Now what is the mechanism by which these persons acquired their increased capacity for color perception? It is not known exactly. Certainly no new structural elements were developed in the retina, nor were any new visual pigments formed. It was probably purely an educational process, teaching the mind to recognize certain visual stimuli in terms of color. Not much is known about the process of color rehabilitation, but how much is really known of the mechanism of color vision in the normal person?

There are many theories of color vision. Psychologists swear by the Hering and Ladd-Franklin theories, physicists swear by the Young-Helmholtz theory, and physiologists, taking an over-all view, swear at all of them. Some recent work on color vision suggests that color perception is not an all-or-none phenomenon. There may be a gradation in color vision, corresponding somewhat to the gradation in form vision. Form vision ranges from a maximum of 20/15 or 20/10 to a minimum of 20/200 or less. Probably color vision likewise ranges from a high level embracing the capacity to distinguish a great many colors, shades and tints to total

² Huxley, A. L. *The Art of Seeing*, New York, Harper & Bros. 1942.

³ Pascal, J. I. On Aldous Huxley's "The Art of Seeing," *Am. J. Ophth.* 26: 636 (June) 1943.

deficiency in color vision. Between these are the color amblyopias of varying degree, corresponding to the form amblyopias of varying degree. Just as one can in many cases remove or improve a form amblyopia, so one may be able to improve a color amblyopia. This, I believe, is a justifiable open-minded attitude.

A type of visual exercise which is practiced more by teachers and educators generally than by ophthalmologists concerns improvement in the speed of reading. There are several instruments designed specifically for this purpose. But even without elaborate instruments one can teach patients, to some extent at least, the art of rapid reading. Many a student who had unwittingly acquired a habit of reading slowly, say, 200 words a minute, can, by being prodded and urged and by making an effort, increase his speed to 300 or more words a minute. In these days, when every intelligent student and adult has far more reading than he can ever hope to do, the acquisition of skill in rapid reading is certainly a worth while accomplishment.

Akin to this type of visual exercise, but much more developed and on a broader psychologic basis, is the work being done now at Ohio State University by Dr. Samuel Renshaw and his associates. Primarily, their training is to increase the speed and span of the visual act. Exercises for this purpose have been used and found effective by some branches of the armed services. But rapid and extensive visual recognition is certainly a worth while skill in many lines of civilian endeavor. The work of Dr. Renshaw has shown to what an amazing extent this faculty can be developed by proper training. Incidentally, this work has wider implications than those I have mentioned. Ramifications of it reach, though by a different route, some of the practices of the so-called Bates system.

Visual exercises which are most familiar to ophthalmologists relate to the development of improved neuromuscular coordination of the two eyes. This is the well known field of orthoptics, in the restricted sense of the term. I shall merely mention one or two points bearing on this work. Manifest deviations, actual squints, are relatively rare as compared with the number of latent deviations. Orthophoria is the exceptional finding, some horizontal and, less commonly, some vertical heterophoria being the rule. Now, when a patient with a refractive error shows also an appreciable amount of heterophoria, what is the physician to do? One way is to correct the ametropia, ignore the heterophoria and wait a

month or two. If the patient's complaints of discomfort persist after correction of the ametropia, then the physician must attend to the heterophoria.

Another way is to make the red glass test before prescribing the lens correction. If with mere discoloration of the images, preferably that of the nondominant eye, dissociation and diplopia result and if, in addition, the images stay apart or come together slowly, then the imbalance is likely to be a factor in the patient's discomfort. In such cases it is advisable to do something about the imbalance at the time of correcting the ametropia.

There are two ways of treating the imbalance. One is to incorporate a prism for relief. Another and, whenever possible, a better way, is to give a series of visual exercises in order to build up fusion and reserve duction power. Dr. Burian's work on the importance of peripheral stimuli in the development and maintenance of fusion has clarified many puzzling points in fusion training. In fact, targets for these exercises should be made on the basis of Dr. Burian's findings.

Now and then one reads in the lay, and sometimes in the professional, press of eye exercises consisting of wall to wall and floor to ceiling movements. I think such exercises are senseless, for these movements are constantly being made in the ordinary course of daily use of the eyes. What is needed are movements which are not ordinarily made—and these are primarily forced duction or vergence movements in which the eyes are made to move in opposite directions. These exercises build up reserve power, but they are not muscle exercises. They are, rather, procedures for developing smooth neuromuscular pathways, probably akin to conditioned reflexes.

There are many elaborate instruments for use in training, but these exercises can also be effectively given by the application of simple prisms. These prisms can be employed in a variety of ways to provide rhythmic or sustained exercises, with use of the step method or the sliding method or a combination of the two. In all cases, however, the eyes should be made to execute various conjugate movements while under the tension of the prism. A simple stereoscope can also be of aid and is especially effective when used with the pointer method, a procedure which I first described about twelve years ago.⁴

⁴ Pascal, J. I. Visual and Orthoptic Training, Am J Ophth 17:801 (Sept) 1934.

CONCLUSION

I believe that all these visual exercises belong in the domain of ophthalmology. But not every ophthalmologist is fitted either by temperament or by inclination to engage directly in this work. For the training is largely in the nature of teaching and requires special aptitude and skill on the part of the teacher. A man may be a first rate ophthalmologist and a third rate teacher. It is at this juncture that the orthoptic technician comes to the fore. Such a technician can be

trained to apply intelligently all these varieties of visual exercise under the supervision of the ophthalmologist. The fact that these technicians are mostly women is probably not an accident. Women usually excel in teaching elementary skills, they generally have more patience, tact and enthusiasm for the work. But in all cases their work should be under the critical supervision of a well informed ophthalmologist who is in sympathy with this type of work.

37 West Ninety-Seventh Street

Clinical Notes

A MODIFIED SLING OPERATION FOR CORRECTION OF PTOSIS

JOSEPH LAVAL, M.D., NEW YORK

For the correction of ptosis in the absence of action of the levator muscle two procedures are open to the surgeon. One is to utilize the superior rectus muscle if it is active, as in the Motaïs procedure,¹ and the other is to make a sling which will lift the lid, as in the Machek

in which the skin of the upper lid is utilized for the sling. Instead of utilizing skin of the upper lid for the sling, Derby,⁴ and later Wiener and Alvis,⁵ used fascia lata.

In 1924 Reese⁶ suggested using strips of orbicularis muscle and pretarsal fascia to pro-

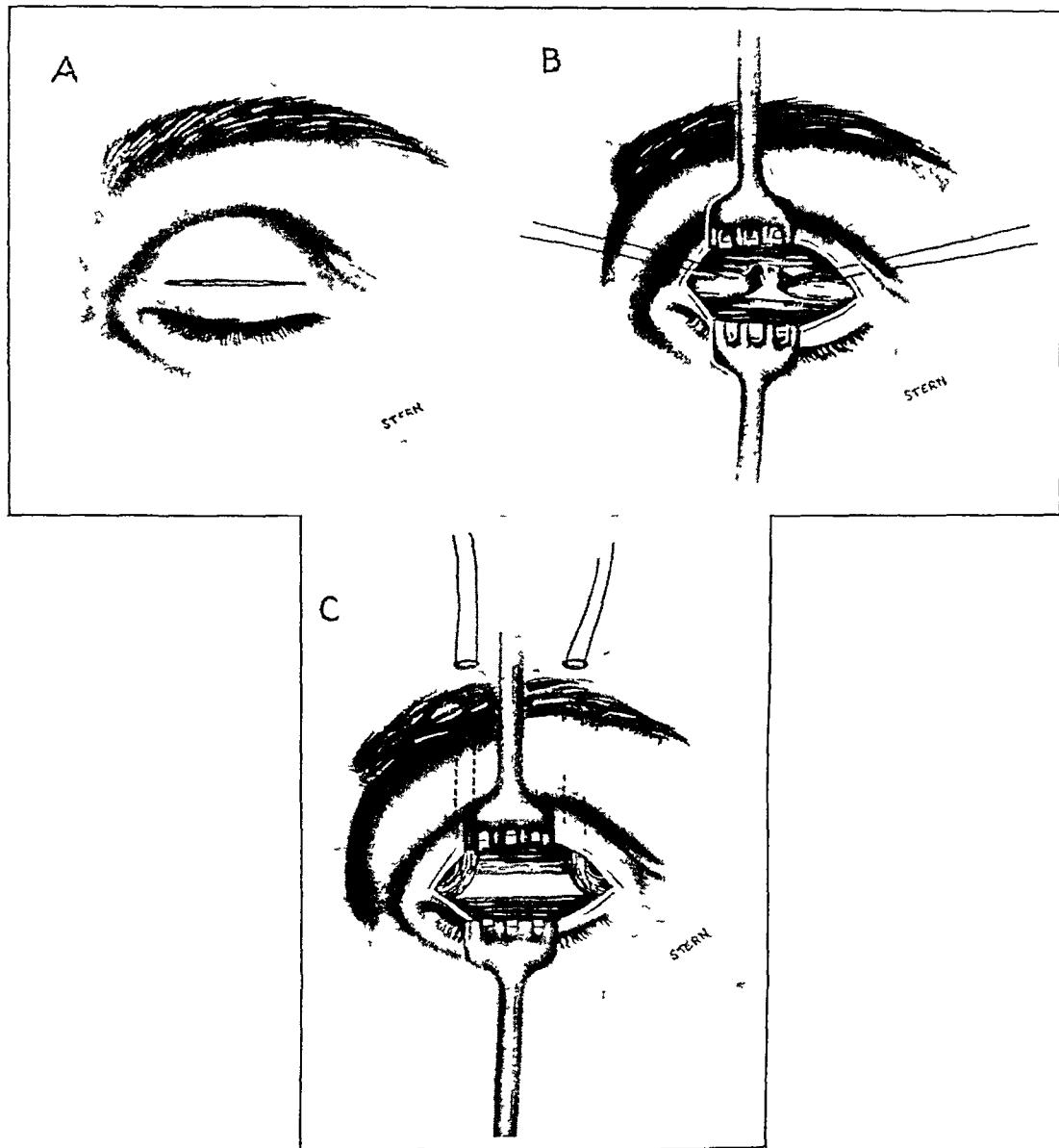


Fig 1.—Stages in the sling operation for correction of ptosis

procedure,² when the superior rectus muscle is paralyzed. The latter method is a modified Panas operation³ or a Hunt-Tansley procedure,

1 Motaïs Operation du ptosis par la greffe tar-sienne d'une languette du tendon du muscle droit supérieur, Bull et mem Soc franç d'opht 16 199, 1898

2 Machek An Operation for Ptosis with the Formation of a Fold in the Upper Lid, Arch Ophth 44 539, 1915

3 Panas, P Traité des maladies des yeux, Paris, G Masson, 1894

4 Derby, G S Correction of Ptosis by Fascia Lata Hammock, Am J Ophth 11 352, 1928

5 Wiener, M, and Alvis, B Y Surgery of the Eye Philadelphia, W B Saunders Company, 1939, p 326

6 Reese, R G Operation for Blepharoptosis with Formation of a Fold in Lid, Arch Ophth 53 26, 1924

duce a sling I have simplified and modified his procedure, as described here.

An incision is made through the skin and subcutaneous tissue of the upper lid 2 mm above the tarsal edge (fig 1A). The incision extends the full width of the lid, and the margins are dissected free from the underlying orbicularis muscle. The latter is then lifted up with forceps, and a strip 3 mm wide is prepared just above the upper tarsal margin. This strip extends the full width of the lid, just as the original incision in the skin was made. The temporal and nasal attachments of the strip of orbicularis muscle are not dissected but are left in position. The strip of muscle is cut in half at its center, and a mattress suture of braided silk on a full curved needle is passed through each cut end (fig 1B). (In the Reese procedure the orbicularis

a continuous fine silk suture on anatraumatic needle (In the Reese procedure an anchor suture is taken through the center of the tarsal tissue of the lid and brought out on the brow, the sutures through the strips of orbicularis muscle are not attached to the periosteum but are brought directly through the incision in the skin above the eyebrow) A Wheeler cone is then applied and left in place for five days, at the end of which time the running suture in the lid is removed. On the seventh day the silk sutures which hold the strips of orbicularis muscle attached to the periosteum are removed.

This procedure is recommended in cases in which the levator and the superior rectus muscles are completely paralyzed. If the levator muscle is active to any degree, a resection of this muscle



Fig 2.—At left, appearance before operation. At right, left eye two weeks, and right eye two months, after operation.

muscle plus fascia is dissected and the lateral ends are freed, the central portion remaining attached.) Two tunnels are then dissected under the skin of the upper lid to the brow, emerging through the skin just above the eyebrow. One tunnel is along the nasal portion and the other along the temporal portion of the lid, and the two tunnels proceed straight upward. The full curved needles of one strip of orbicularis muscle are then passed through the corresponding tunnel and deep bites taken down to the periosteum and out through the skin of the exit of the tunnel. The same procedure is carried out with the needles of the other strip of orbicularis muscle (fig 1C). The sutures are then drawn as tight as possible and tied over rubber pegs. The incision through the skin of the lid is sutured with

is by all means the operation of choice. If the superior rectus muscle is active, a Mota's or a Wheeler⁷ operation, using a sling of orbicularis muscle under the superior rectus muscle, is advocated. Dickey⁸ uses a sling of fascia lata which he attaches to the superior rectus muscle.

136 East Sixty-Fourth Street

7 Wheeler, J. M. Correction of Ptosis by Attachment of Strips of Orbicularis Muscle to Superior Rectus Muscle, *Arch Ophth* 21:1 (Jan) 1939.

8 Dickey, C. A. Superior-Rectus Fascia-Lata Sling in Correction of Ptosis, *Am J Ophth* 19:660, 1936.

Correspondence

ILLUMINATION FOR THE OPHTHALMOLOGIST

To the Editor—In the January 1945 issue of the ARCHIVES, page 1, appeared a lucid and simplified discussion on "Elementary Illumination for the Ophthalmologist," by Dr Legrand H Hardy and Dr Gertrude Rand. The subject was thoroughly covered. There is, however, one point with reference to the units employed in illumination which, in my experience, has proved a stumbling-block to ophthalmologists and which can, perhaps, be still more simplified. This pertains to the difference and/or the relation between the foot candle (or the meter candle, or lux) and the lumen.

It is, of course, more scientific to define the foot candle in terms of the lumen, but it is easier to understand both by regarding them as different, in some such way as this. The foot candle may be thought of as a unit of "light pressure," or "light density," or "intensity of concentration of light," as Drs Hardy and Rand phrased it. The foot candle is most simply and commonly defined as the illumination received on a surface which is 1 foot from a light source of 1 candle power. On every point of such a surface there is 1 foot candle of light pressure, or light concentration.

The lumen is best thought of as a unit of the amount or quantity of light received on a unit area of a surface, the light pressure or light concentration on which is given in terms of foot candles, or meter candles. One lumen is the quantity of light received on 1 square foot of a surface which has an illumination (light pressure) of 1 foot candle. In some rough way, this is analogous to what almost every one is familiar with in electricity. The volt is a unit of electrical force, or pressure, and the ampere is a unit of the amount of electricity.

Thus, on a surface which has an illumination of, say, 10 foot candles, i.e., a light pressure of 10 foot candles, each square foot has an illumination of 10 lumens. One-half a square foot has an illumination of one-half this (5 lumens of light), and one-tenth square foot has an illumination of one-tenth this, i.e., 1 lumen. But the one-half square foot and the one-tenth square foot both have the same light pressure, i.e., 10 foot candles.

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Book Reviews

The March of Time The New York Academy of Medicine Lectures to the Laity Price \$1.75 Pp 121 New York Columbia University Press, 1945

The ninth annual series of lectures on timely subjects to the laity by prominent leaders are now made permanent and available to a larger circle of readers by this publication of the New York Academy of Medicine.

After a foreword by Dr Arthur F Chace, the president of the Academy, and an introduction by Dr Harold R Maxwell, chairman of the committee on medical information, the six lectures follow.

The subjects of the lectures are as follows: "Morale and Propaganda," Dr Edward A Strecker; "Food and Civilization," Dr Charles G King; "The Past, Present and Future of Chemotherapy," Dr Colin M McLeod; "Medicine and the Changing World," Dr Reginald Fitz; "The Effects of Science upon Human Beings," Sir Gerald Campbell, and "Wars and Epidemics," Lieut Col Thomas T Mackie.

This is an admirable collection of topics, both for their timeliness and for the excellent selection of the subject matter.

These lectures help to keep up the educational value which the series have attained in previous years. The present lectures relate to this war period and the changing world, and the thoughtful reader will be well repaid by their perusal.

ARNOLD KNAPP

Eye, Ear Nose and Throat Manual for Nurses
By Roy H Parkinson, M.D., F.A.C.S. Fifth edition Price, \$2.25 Pp 247, with 82 illustrations, 2 in color St Louis C V Mosby Company, 1944

This manual was favorably reviewed in the ARCHIVES (17.388 [Feb.] 1937). It has now been brought up to date, with a small increase in the number of pages and the addition of a number of new illustrations. It should continue to be popular and useful.

ARNOLD KNAPP

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Conjunctiva

OBSERVATIONS ON THE TRANSPARENCY OF THE CONJUNCTIVA P A GARDINER, Brit J Ophth 28: 538 (Nov) 1944

The aim of the author is to define the normal appearance of the conjunctiva and to elucidate, if possible, the causes of deviations from the normal, with particular reference to the part nutrition might play

Slit lamp examination was made of large numbers of subjects of both sexes of different nationalities, living in different climatic conditions and on different diets. The ages ranged from 9 to 37 years. Experiments were performed on several groups of subjects.

The anterior half of the nasal and temporal segments of the interpalpebral bulbar conjunctiva was examined with the slit lamp. The following conclusions are arrived at:

The transparency of the interpalpebral bulbar conjunctiva increased between the ages of 9 and 37 years in the absence of hyaline degenerative changes. In those subjects in whom hyaline degenerative changes were found, the areas which were spared showed increased transparency with age.

The rate of change was most rapid between the ages of 17 and 30 years and was less at the two extremes of the age range examined.

The females examined showed a constantly more transparent conjunctiva than males between the ages of 9 and 27 years.

Nutritional factors probably play a part in influencing the transparency of the conjunctiva. A good diet tends to increase opacity whereas a bad diet increases transparency between the ages of 9 and 37 years.

There was an association, probably through nutrition, between the transparency of the conjunctiva and increased vascularity of the limbus. Slit lamp examinations of the conjunctiva of a group of subjects enable deductions to be made as to nutritional well-being of the group.

W ZENTMAYER

Cornea and Sclera

EFFECT OF RIBOFLAVIN ON CORNEAL VASCULARIZATION AND SYMPTOMS OF EYE FATIGUE IN ROYAL CANADIAN AIR FORCE PERSONNEL F F TISDALE, J F McCREARY and H PEARCE, Canad M A J 49: 5 (July) 1943

Tisdale and his collaborators attempted to demonstrate photographically the changes which

occur in the cornea in riboflavin deficiency. Kruse and his co-workers had suggested that the minor degrees of vascularization of the cornea frequently seen in apparently normal human beings were due to a deficiency of riboflavin. They postulated that symptoms of tiredness of the eyes, burning of the eyes, a sandy sensation under the lids and lacrimation might be manifestations of the deficiency and might be cleared by the administration of riboflavin. Riboflavin is rapidly destroyed by light, and it seems possible that a person who is exposed to a great deal of light would have an increased destruction of riboflavin in the eye, which would necessitate a greater intake to maintain normal vision and health. Men in the air forces are exposed to much light. The authors investigated the various degrees of vascularization of the cornea in men who were flying over water and exposed to considerable glare. One hundred and ninety-eight men were examined. Only 1 man had normal eyes, 17 showed stage 1 involvement, 87 had stage 2, and 93, stage 3. A group of men showing stage 3 involvement were chosen to demonstrate the effect of treatment on vascularization of the cornea and the symptoms of fatigue of the eyes. These men were questioned regarding tiredness of the eyes, aching of the eyes, watering of the eyes, sandy sensation under the lids, dizziness, headaches, intolerance of reading and decreased visual acuity. Sixty-seven per cent had two or more of these symptoms. The men were divided into three groups. One group received capsules containing 3.3 mg of riboflavin three times daily for two months, the second group received similar capsules three times daily for one month, and the third group received capsules which were similar in appearance but which contained no riboflavin. Of the 28 men who received treatment with 9.9 mg of riboflavin daily for two months, 20 showed either pronounced or moderate improvement, 8 showed either slight or doubtful improvement or no change, and none showed increase in vascularization of the cornea. Of the 21 men who received treatment for one month, 6 showed pronounced or moderate improvement, 14 showed slight or doubtful improvement or no change, and 1 man showed an increase in vascularity. Of the 21 men treated with placebos, none showed either pronounced or moderate improvement, 15 showed slight or doubtful improvement or no change, and 6 were worse. In areas where milk, the best source of riboflavin in the diet, was not

available the prevalence and the severity of corneal vascularization were increased

J A M A (W ZENTMAYER)

HERPES CORNEAE AND VIRUS INFECTION A
LOEWENSTEIN Glasgow M J 141 54 (Feb)
1944

This discussion of herpetic keratitis and virus infections of the eye, by Prof A Loewenstein, of Prague Czechoslovakia, was delivered as a postgraduate lecture on Sept 15 1943, at the Tenment Institute of Ophthalmology, University of Glasgow. Loewenstein gives a historical survey of herpes corneae, beginning with the demonstration seventy years ago by Horner of the specific nature of corneal ulci combined with anesthesia of the cornea and continuing with the demonstration in 1911 by Grueter of the transmissibility of corneal herpes to the cornea of rabbits. The pathology of the disease is discussed with particular reference to the relation of the virus to the corneal nerves and to the intranuclear inclusion bodies. Histologic studies by the author failed to demonstrate any damage to the nerve fibers in the experimental disease in rabbits but the linkage of hypesthesia or anesthesia to all clinical forms of human herpes of the cornea makes the presence of such damage probable. The author explains the difference between spontaneous herpes of the human cornea and inoculation herpes of the rabbit cornea on the basis of differences in the nerve fiber patterns the nerve fibers in the human cornea showing dichotomous branching without anastomoses and the nerve fibers in the rabbit cornea showing numerous anastomoses.

The author states that one type of herpes zoster ophthalmicus, herpes iridis Macheck, or iritis herpetica is restricted to mesodermal tissue. It is an iritis beginning with neuralgia of the first branch of the trigeminal nerve with or without typical cutaneous involvement, and including swelling of the iris tissue roseola and hyphemia. Extensive vitiligo of the iris may occur. The relationship of this virus to the virus of chickenpox is noted and the occurrence of a typical case of vitiligo iridis accompanying chickenpox is described.

Brief surveys of other virus diseases, including smallpox, epidemic keratoconjunctivitis measles verruca molluscum contagiosum, lymphogranuloma venereum trachoma and inclusion conjunctivitis, are presented

PHILLIPS THYGESEN

THE CORNEAL GRAFT FROM CADAVER CORNEA
PEREZ-BUFL Arch Soc de oftal hispano-am 3. 464 (Nov-Dec) 1943

Perez-Bufl's first experience in corneal grafting operations was in 1906 when he used heteroplasty, with poor results. Later he used hemokeratoplasty experimentally, having obtained the

best results with crossed sutures from limbus to limbus to hold the transplant. In his experience Castroviejo's continuous suture has produced a severe keratitis, which interferes with healing.

An operation was performed on a woman aged 45 with total leukomas of both corneas. The transplant was obtained from a cadaver twenty-four hours after death. A cataractous lens was found behind the opaque cornea. Although the prognosis was considered unfavorable, the girl took, and sixteen months after the operation vision has improved to ability to count fingers at 60 cm and the perception of colors. Further improvement is expected.

In a second case, operation was performed on a woman aged 50 with sclerosing keratitis. The donor was a three months premature baby who had died nine hours before. This patient's vision was also improved notwithstanding the presence of lesions in the fundus.

H F CARRASQUILLO

Experimental Pathology

**CORNEAL HEALING ADHESIVE POWER OF
AQUEOUS FIBRIN IN THE RABBIT** A L
BROWN and F A NANTZ Am J Ophth 27
1220 (Nov) 1944

Brown and Nantz give the following summary:

"1 The wound edges after an incision in the rabbit cornea are approximated strongly by the secondary aqueous."

"2 A wound surrounding a transplant will support 11,000 times the weight of the transplant in four hours.

"3 This sealing is accomplished by the fibrin produced in the aqueous."

"4 The aqueous fibrin is a product of the union of thrombin from the wound edges and fibrinogen in the aqueous."

"5 Heparin was injected into the anterior chamber to replace aspirated aqueous. This agent markedly decreased the adhesive power of the secondary aqueous after corneal incision."

"6 The heparin was then replaced by thrombin-fibrinogen and the adhesive power was restored."

"7 No comparable action occurs in man. There is no more than a trace of fibrinogen in human aqueous and a correspondingly diminished adhesive power."

W S REESE

CHANGES IN THE INDEX OF REFRACTION IN THE OCULAR MEDIA IN ANIMALS SUBJECTED TO THE ACTION OF SULFONAMIDE COMPOUNDS
J PEREZ LLOVEA and J J ALMEJARA Arch Soc de oftal hispano-am 3 425 (Nov-Dec) 1943

The presence of slight transitory myopia during the course of sulfonamide therapy has been

observed in recent years. The authors have conducted experiments on animals to determine whether the presence of these compounds in the ocular media in vitro could bring about changes in their index of refraction capable of explaining the myopia observed clinically.

The result of their observations was that the changes in the refractive index of the media of eyes under experimentation was so slight that the clinical observations could not be attributed to that change. Changes in the refractive index occurred only in the fifth cipher in concentrations which could be obtained in patients receiving sulfonamide therapy. H F CARRASQUILLO

General Diseases

A CASE OF POLYCYTHAEMIA VERA—EXTRACTION OF BOTH LENSES SATISFACTORY RESULT J C MARSHALL, Brit J Ophth 28: 481 (Oct) 1944

Marshall successfully removed a cataract from each eye of a man aged 74 with polycythemia vera. The blood count revealed 7,250,000 red cells and 12,000 white cells.

Ophthalmoscopic examination of the right eye was impossible, owing to "advanced cataract." In the left eye the disk was suffused, and there was a hemorrhage at the macula. The resulting visual acuity was 6/6 in each eye. In the right eye there was a patch of old choroiditis, resembling Tay's choroiditis, which was outside the macula. Care must be taken not to confuse the condition with that of a cerebral tumor associated with headache and papilledema.

W ZENTMAYER

CHILOMOTHERAPY OF TUBERCULOSIS OF THE EYE

REPORT OF CASES A MIKLÓS, Klin Monatsbl f Augenh 106: 20 (Jan) 1941

Miklos reviews the use of metals, especially gold, in the treatment of tuberculosis of the eye. The results were not encouraging. Toxicity was observed, involving the liver, digestive tract, skin and kidneys. A new combination, rubrophen, was used with success at the ophthalmic hospital of the University of Debrecen (Hungary) for a number of years.

Rubrophen consists of trimethoxydioxoxtotri-tan ($C_{22}H_{20}O_6$). Fifty patients were treated—3 with chronic iridocyclitis, 9 with iritis, with subacute iridocyclitis, 5 with sclerokeratitis, 1 with sympathetic ophthalmia, 2 with perivasculitis retinalis, 2 with choroiditis, 3 with tuberculous keratitis, and 20 with severe eczematous keratoconjunctivitis. A number of case histories are discussed. Rubrophen proved its value for several forms of tuberculosis of the eye, improvement becoming evident swiftly in some of them. Results showed slowly after several months, in some patients with iridocyclitis. The application of rubrophen should not be discontinued after

initial failure in treatment of uveitis, sympathetic ophthalmia, angiopathia retinae and other chronic inflammations.

Recurrences took place at longer intervals, although they might occur after apparently complete recovery. The author agrees with other writers, who recommend that for several years after recovery rubrophen be used during the favorable seasons, spring and fall. Rubrophen, like tuberculin, has to be used for long periods.

K L STOLL

Glaucoma

TENOTOMY OF THE RECTUS MUSCLES IN GLAUCOMA A GARTNER and R K LAMBERT, Am J Ophth 27: 1228 (Nov) 1944

Gartner and Lambert report 2 cases of absolute glaucoma in which they tenotomized the rectus muscles, causing a temporary reduction in tension. In the first case there was a reduction in tension of from over 70 to 50 mm of mercury (Schiotz). The reduction lasted six weeks and was followed by a gradual increase to 70 mm of mercury in three months. In the second case the eyeball was stony hard. The cornea was gray and vascular. The surface was irregular and presented vesicles. After the operation the corneal condition improved. Tension was 34 mm of mercury for over six weeks and then rose to 40 mm, where it stayed for the three months prior to the time of the report. The patient was much relieved by the operation. The authors state that they were unaware when they performed the operations that Sapir had used the same procedure in 43 cases of various types of glaucoma.

W ZENTMAYER

NOTES ON AN OPERATION FOR GLAUCOMA R J MASTERS, Am J Ophth 27: 1371 (Dec) 1944

Masters describes an operation which he has been performing for ten years. It is a combination of cyclodialysis, iridectomy and fistulization, the formation of a fistula being effected by a ragged, flaplike incision. This paper is a preliminary report.

W S REESE

Injuries

TRAUMATIC ENOPHTHALMOS J L MALBRAN and F GARCIA NOCITO, Arch de oftal de Buenos Aires 18: 655 (Dec) 1943

The authors report 7 cases of this symptom complex and state that a total of 157 cases appear in the literature. Males are more likely to be affected than females. The condition is chiefly seen in youth and mature life, but a case of a patient 12 years old and another of 60 have been reported. The syndrome may be produced by several types of wounds, but contusion in the

neighborhood of the orbit is particularly likely to cause it. Cases in which the globe is dislocated after destruction of the orbital walls are not included.

Usually, the syndrome makes its appearance a few weeks after the trauma, but in some cases it has occurred as early as six hours afterward and in others one year later.

The amount of enophthalmos usually averages 3 to 5 mm., but as much as 35 mm. has been seen.

The appearance is that of an artificial eye, as the fold in the upper lid is lost. Paralysis or paresis of the muscles frequently accompanies the condition. In about half the cases reported vision was preserved, in the others visual acuity was diminished even to complete blindness. The visual field may be contracted. In some cases a central scotoma is present. The pupil is usually dilated, fixed miosis is the exception. Accommodation may be normal or altogether paralyzed. Hypotension, trophic disturbances of the same side of the face and paresthesias in the region of distribution of the trigeminal nerve are frequent. Lesions in the lacrimal apparatus also occur.

As to the theories of its causation, rupture of the trochlea and a lesion of the sympathetic fibers have been mentioned. Enlargement of the osseous cavity of the orbit by fracture or by atrophy of the retrobulbar tissue, cicatricial retraction and destruction of the suspensory ligaments of the eye have also been considered causative factors.

The authors give in detail the history and findings in the cases which they studied and a summary of the cases reported in the literature.

H F CARRASQUILLO

PROSTHESES AFTER MILITARY TRAUMA OF THE ORBIT D SUDAKEWITCH, *Vestnik oftal* 22: 25, 1943

The orbital injuries during the Russo-Finnish war constituted about 11 per cent of all orbital injuries. Sudakewitch classifies orbital injuries as (a) orbital, (b) orbitalfrontal, (c) orbitalnasal and (d) orbitalzygomatic, a classification which is correlated with the functional-topographic character of the orbital and the adjacent cavities and with the material of which the prostheses are made.

In the repair of orbital injuries the prosthesis should be firm and nonflexible. For orbitalzygomatic injuries the prosthesis should be of elastic material, because of the many muscles attached to the zygoma and cheek, for fronto-orbital and frontonasal injuries the prosthesis should be thin but nonelastic. A combination can be used, according to each individual case.

O SITCHEVSKA

Lacrimal Apparatus

PERMEABILIZATION OF THE LACRIMAL PASSAGES A P GUILLEM, *Arch Soc de oftal hispano-am* 3:487 (Nov-Dec) 1943

Instrumental dilation of the lacrimal passages produces an anatomic alteration of the walls of these passages, and the condition of epiphora persists. With the aim of conserving the anatomic integrity of these passages, the author uses electrocoagulation. Thirty-one patients have been treated successfully. A fine lacrimal sound with an insulating covering, except at its tip, is used to catheterize the passages. When the obstruction is encountered, the circuit is made for a short time, a current of 80 to 100 milliamperes being used, and the sound is pushed in. After this initial permeabilization, dilation is performed daily for eight or ten days.

H F CARRASQUILLO

Neurology

MECHANISMS OF HEADACHE H WOLFF, *Arch Neurol & Psychiat* 50: 224 (Aug) 1943

This excellent review summarizes the author's extensive investigation of this subject.

Six basic mechanisms for headache from intracranial sources are formulated: (1) headache from traction on veins that pass to the venous sinuses and from displacement of the great venous sinuses, (2) traction on the middle meningeal arteries, (3) traction on large arteries at the base of the brain and their branches, (4) distention and dilatation of intracranial arteries, (5) inflammation in or about any of the pain-sensitive structures of the head, and (6) direct pressure by tumors on cranial or cervical nerves containing pain afferent fibers from the head.

The author defines the pain-sensitive structures of the head as (1) all tissues covering the cranium, particularly the arteries, and (2), of the intracranial structures, the great venous sinuses, parts of the dura at the base, the dural arteries and cerebral arteries at the base of the brain, the fifth, ninth and tenth cranial nerves and the upper three cervical nerves.

Stimulation of pain-sensitive structures on or above the superior surface of the tentorium cerebelli resulted in pain in various regions in front of a line drawn vertically from the ears across the top of the head, the pathways for this pain being contained in the fifth cranial nerve.

Stimulation of pain-sensitive structures below the inferior surface of the tentorium cerebelli resulted in pain in various regions behind the aforementioned line, the pathways being contained in the ninth and tenth cranial and the upper three cervical nerves.

The investigator suggests that headache associated with increased or decreased intracranial

pressure results from traction on or displacement of pain-sensitive intracranial structures and is independent of changes in pressure of themselves

The localizing value of headache associated with tumor of the brain as it pertains to the position of the tumor is reviewed

Wolff then discusses histamine headache, headache associated with fever, migraine headache, headache associated with hypertension, and the muscles of the scalp and neck as sources of pain

With relation of headache to the eyes, investigations were made on pain-sensitive structures, superficial and deep, of the eye, on the headache and aching of eyes associated with refractive errors and imbalances of the extraocular muscles, and on photophobia. Increased intraocular pressure produced a sharp pain which at first remained localized, but later extended along the rim of the orbit and finally involved most of the area supplied by the ophthalmic division of the trigeminal nerve. Experimentally induced hyperopia and astigmatism caused headache, while induced myopia did not. Induced imbalance of the extraocular muscles caused tension and irritability and, if prolonged headache developed, abnormal electromyograms from the muscles of the scalp and neck. Normally occurring muscle imbalances produced similar symptoms and myograms.

Finally, the pain associated with nasal and paranasal structures is discussed—"the sinus headache." Inflammation and engorgement of turbinates, ostiums, nasofrontal ducts and superior nasal spaces are responsible for most of the pain radiating from the nasal and paranasal structures. If headache is not associated with engorgement and inflammation of the turbinates, it is in all probability not a result of disease of the nasal or paranasal structures. Furthermore, if headache in the zygomatic, frontal or temporal region or over the vertex is not greatly reduced in intensity or eliminated by shrinkage or local anesthetization of nasal structures, it is in all probability not due to disease of the nasal or paranasal structures.

R IRVINE

**OCULAR SYMPTOMS OF THE "SACRED DISEASE"
[EPILEPSY]** R ARGAÑARAZ, Arch de oftal de Buenos Aires 18: 546 (Nov) 1943

The author gives the following ocular symptoms of epilepsy (called the "sacred disease" by Hippocrates) enlargement of the blindspot of Mariotte and contraction of the internal isopters of 2/2000, congestion or true neuritis, and either primary or secondary atrophy of the optic disk. Attention is called to the fact that these findings are not mentioned in any textbook. Epilepsy should be diagnosed by the oculist.

Seven cases are presented to illustrate these features. Campimetric illustrations appear in the article.

H F CARRASQUILLO

Ocular Muscles

CONGENITAL PARALYSIS OF BOTH EXTERNAL RECTI TREATED BY TRANSPLANTATION OF EYE MUSCLES J A MAGNUS, Brit J Ophth 28: 241 (April) 1944

Magnus operated on a patient with bilateral abducens paralysis and pronounced right hyperphoria due to an overacting right inferior oblique muscle. The O'Connor technic of transplantation was used. The cosmetic effect was satisfactory, but abduction was practically impossible. An unusual finding was abnormal thickness of the external rectus muscle, with an abnormal anatomic position of the left eye.

W ZENTMAYER

THE EFFECTS OF FARADICALLY INDUCED CURRENTS UPON THE EXTRINSIC AND INTRINSIC OCULAR MUSCULATURE A CLINICAL SELF EXPERIMENT J H YOUNG, Brit J Ophth 28: 488 (Oct) 1944

Young performed the experiments on himself. The Smart-Bristow electric induction apparatus, with a modification required for the experiments, is described. The phenomena resulting from faradic stimulation of the left internal rectus muscle are reported in detail, the experimental signs and symptoms are briefly recapitulated, and the physiology of the reaction experienced is discussed. Faradically induced electric currents have been shown to be capable of producing three important ocular signs: exophthalmos, nystagmus and spasm of accommodation, all mediated through the autonomic nervous system.

It is considered that with the advent of modern general anesthesia and with due safeguarding as regards the type of patient and the strength of current, with or without the use of homatropine as required, faradism should prove helpful in treatment of the various muscular anomalies resulting from war trauma or those of other origin. It should also prove useful in the diagnosis and prognosis of lesions of the ocular muscles.

W ZENTMAYER

Operations

PLASTIC SPHERES FOR IMPLANTATION INTO TENON'S CAPSULE IN THE FROST-LANG TYPE OPERATION FOR ENUCLEATION OF THE EYEBALL R E WRIGHT, Brit J Ophth 28: 573 (Nov) 1944

Wright uses plastic spheres perforated in two diameters at right angles and fluted on the surface in a sort of basket work pattern. These spheres are anchored to the superior and inferior

rectus muscles by surgical gut passed through the vertical tunnel and to the lateral muscles by way of the horizontal tunnel. The sutures are tied over the top of the globe. A purse string surgical gut suture is then passed round the mouth of the bag, alternate bites of Tenon's capsule and cut muscle extremities being picked up and tied off. The fluting of the globe is intended to supplement the fibrous tissue anchorage which eventually takes place. Nothing but a double shell (reform prosthesis) or a carefully filled plastic prosthesis should be used.

W ZENTMAYER

PREVENTION OF HEMORRHAGIC COMPLICATIONS IN THE ORBITAL ANESTHESIA B CARRERAS Arch Soc de oftal hispano-am 3: 420 (Nov-Dec) 1943

Reference is made to an article in which it is stated that orbital hemorrhage could be avoided by using very fine hypodermic needles (not more than 0.7 mm thick) with a very sharp point.

The method advocated by the author consists in using two hypodermic needles one very fine and pointed for a preliminary subcutaneous injection, and another with a dull point, which is pushed through the previously anesthetized skin into the deep tissues of the orbit. The fluid should be injected ahead of the advancing needle.

The retrobulbar method of anesthesia and that for operation on the lacrimal sac are fully discussed.

H F CARRASQUILLO

Pharmacology

EFFECT OF YEAST EXTRACTS ON LOCAL ANESTHETIC ACTIVITY OF COCAINE E S COOK, Proc Soc Exper Biol & Med 54: 203 (Nov) 1943

"Addition of a yeast extract to cocaine hydrochloride solutions reduces the corneal anesthetic potency, this reduction being especially notable when the p_H of the treated solution is lowered to the level of the control solution. There is evidence that the subcutaneous toxicity of cocaine is also decreased by the extract."

P C KRONFELD

THE DIONIN EFFECT IN THE CONJUNCTIVA A LOEWENSTEIN, Brit J Ophth 28: 622 (Dec) 1944

The observations of Loewenstein confirm previous reports that perivascular lymph vessels are commonly observed in cases of subconjunctival hemorrhage four or five days after its occurrence. They can be seen to accompany conjunctival vessels which cross the area of hemorrhage. The width of the sheath on each side of the vessel is approximately equal to that of the blood column and is sharply defined. It is assumed that the whitish yellow sheaths surrounding the vessels within the hemorrhagic area are lymph paths.

They can be visible only when the hemorrhage is confined to the plane of the vessels. If the hemorrhage were superficial, it would conceal both the blood column and the lymph sheath, if it were deeper, it would form a dark background to the vessel and obscure the white sclera, which is essential to render visible the transparent lymph space. The lymph vessels disappear in from forty to sixty seconds after the instillation of a solution of ethylmorphine hydrochloride, concurrently with the onset of the conjunctival edema, and reappear in from thirty to fifty minutes as the edema passes off. The edematous fluid in the conjunctiva, at first clear, becomes milky after fifteen to thirty minutes.

The article is illustrated

W ZENTMAYER

Physiology

FUNCTIONAL POLARIZATION IN RETINAL DEVELOPMENT AND ITS REESTABLISHMENT IN REGENERATING RETINAE OF ROTATED GRAFTED EYES L S STONE, Proc Soc Exper Biol & Med 57: 13 (Oct) 1944

When the eye of the adult salamander is grafted or when its blood supply is temporarily interrupted, the retina always degenerates and regeneration occurs from surviving peripheral cells. When the optic nerve is cut without interference with the blood supply to the retina, the retina survives and the nerve immediately regenerates.

In animals subjected to one of these procedures the visuomotor responses to lures approaching any of the four quadrants of the field of vision and to a rotating black and white drum were studied. Normally the animal moves toward, snaps at and follows the lure and moves automatically head and body in the same direction as the drum when the latter rotates temporonasally through the field of vision.

In one group of animals, one eye was merely turned upside down (180 degree rotation of all quadrants) and fixed in the new position after the conjunctival and muscular attachments were cut without injury to the optic nerve or to the blood supply of the retina. Thus the animal retained its original intact retina, but the localizing functions of each quadrant became reversed. When the lure was brought into the field of each of the four retinal quadrants, the animal reversed its reactions and sought for the lure in the opposite direction. When the eye was rotated back to its normal position, normal visuomotor reactions were restored.

When the eye was excised and reimplanted upside down, return of vision through the new retina showed complete reversal of the localizing function of each retinal quadrant, as in the case of the rotated eye retaining its original retina. Reversal of the localizing function in the nasal and temporal quadrants took place only when

the left (or right) eye was excised and grafted on the opposite side so that dorsal and ventral quadrants were normally oriented

These and other experiments indicate that the localizing function of each retinal quadrant is determined by its original position within the eye and is independent of artificial changes of the position of the eye within the orbit. The local signs of the regenerated retina are the same as those of the original retina which it replaces. Experiments are now under way to determine the exact developmental period at which the retinal quadrants become functionally established ("functionally polarized"). A 400 foot (122 meter) motion picture has been made recording these experiments

P C KRONFELD

BACKFLOW PHENOMENA IN AQUEOUS VEINS OF NORMAL AND OF GLAUCOMATOUS EYES
K W ASCHER, Am J Ophth 27: 1074 (Oct) 1944

Compression exerted by means of a minute cotton applicator on the recipient vessel near its junction with the aqueous vein produces either of the following characteristic aspects. The blocked section of the vessel, including the colorless aqueous vein, becomes filled with red blood cells, or the section becomes clearer than it was before the compression started, even almost colorless. As this part of the vessel resembles a transparent glass rod surrounded by semi-transparent, porcelain-like scleral tissue, the effect has been called the glass rod phenomenon, while the opposite aspect, the entrance of red blood cells into a previously clear vessel, is referred to as the negative glass rod phenomenon. The direction in which, after compression of a recipient vessel, red blood cells or clear fluid leaves or enters an aqueous vein depends on the anastomotic pathways available and on the relative pressure potentials in each of them. As soon as the free flow in a vessel section is blocked, the source under high pressure will get priority. Fluid entering the meshwork from the source under lower pressure will be repelled until a new equilibrium has been established. Eyes with primary compensated glaucoma do not show the positive glass rod phenomenon, and the negative glass rod phenomenon regularly encountered in glaucomatous eyes may be considered an early sign of decompression

W ZENTMAYER

Retina and Optic Nerve

PHOTOGRAPHS OF RETINAL DETACHMENT IN APIAKIA BEFORE AND AFTER OPERATION
E ROSEN, Brit J Ophth 28: 554 (Nov) 1944

A woman aged 61 with a mild form of diabetes associated with rather severe hypertension underwent successful operation for cataract in both eyes. Five months after the operation on

the left eye a large detachment of the retina involving the upper nasal field developed. A hole with a crescentic operculum was present. Several electrodes were inserted in the region of the hole. Two and one-half years later visual acuity was 20/25, and the field showed slight concentric contraction. Photographs of the fundus before and six weeks after the operation for the detachment are included

W ZENTMAYER

RETINAL MICRO-ANEURYSMS AND PUNCTATE HAEMORRHAGES A J BALLANTYNE and A LOEWENSTEIN, Brit J Ophth 28: 593 (Dec) 1944

In several recent papers the authors have directed attention to the minute red dots occasionally associated with the retinopathy of diabetes and included with the so-called deep, punctate hemorrhages which form part of the ophthalmoscopic picture of that disorder. It can now be shown that many, if not most, of the so-called punctate hemorrhages characteristically associated with diabetic retinopathy are actually capillary aneurysms.

By examination of the unstained retina in bulk, as well as in vertical and flat serial sections, these bodies are seen to be compact collections of red blood corpuscles, globular, with an average diameter of 50 to 60 microns and enclosed in a wall of varying thickness. With few exceptions, they occur in the inner nuclear layer, in the course of the capillaries which link the deeper and the more superficial capillary plexuses of the retina.

They may be a source of hemorrhage by diapedesis or by rhexis, and many of them are seen to undergo a process of thrombosis and cicatrization. They represent a stage in the vicious circle in which changes in the capillary endothelium lead to stasis in the circulation, which, in turn, causes further vascular changes, especially on the venous side of the retinal circulation.

The article is well illustrated

W ZENTMAYER

Trachoma

ON THE MORBIDITY OF TRACHOMA A DE ROTTH, Am J Ophth 27: 1279 (Nov) 1944

De Rotth gives the following summary:

"Only in communities in which members of families live under very crowded and poor hygienic conditions, can the real sick rate of trachoma be determined, because of the chance of repeated and massive contacts. The morbidity is 100 per cent in Egypt, 30 to 60 per cent in Japan, and was found to be 30 to 58 per cent in Hungary, 42.3 per cent in inclusion-positive trachoma families. Certain individuals and old persons have a relative immunity, but no race is

immune from trachoma. The main source of trachoma is the family, and in southeastern Europe the migratory laborer.

"General welfare and hygiene help in the fight, as is well known. But the most important weapon is the treatment. The disappearance of the inclusion bodies from the conjunctiva in a few days, when sulfanilamide is administered, makes us hope that the infectivity of the individual can be quickly suspended, and thus the danger he represents be eliminated for family and country."

W S REESE

Uvea

GREEN SPOT IN THE FUNDUS OF THE EYE J L PAVIA and R LACHMAN, Arch de oftal de Buenos Aires 18: 647 (Nov) 1943

The occurrence of this sign in the fundus is more frequent than is generally believed. Forty-seven cases have so far been reported, the last 3 of which are mentioned in this paper.

With ordinary light this spot appears as a light green or grayish green area. If the red-free filter is interposed in the Gullstrand ophthalmoscope, the spot is not seen (as only the retina is visualized), and in this way it is differentiated from a retinal pigment deposit or hemorrhage. The best way to observe the green spot is by using the red radiation at the extreme end of the spectrum (the "infra-red Ilfor B filter") or by employing retrotransillumination of the chorioretina obtained with the Oculus ophthalmoscope. The spots are located in the substratum of the choroid.

With the special illumination the green spot has diffuse muddy margins, which fade out gradually and do not stand out prominently from the rest of the fundus; the spot is of irregular thickness and shows indentations and areas of lesser density.

The green spot is differentiated from pigment deposits by the black, discrete appearance of the latter, from choroidal hemorrhages by their deep black color and irregular margins and from intervacular pigment in the choroid by the particular arrangement of the pigment.

The condition is hard to photograph. The technic is given. The authors report 3 cases in which the green spot was present, all of which were seen in patients with cardiovascular disease, 2 with hypertension.

H F CARRASQUILLO

Therapeutics

PENICILLIN IN OPHTHALMOLOGY J G MILLER, Brit M J 2: 175 (Aug 5) 1944

This report includes a series of cases studied by various observers. Penicillin was used in the

strength of 500 units per cubic centimeter when given in the form of drops and of 100 units per gram when used in an ointment base of lanette wax and petrolatum. Penicillin will retain its potency in the drop solution for four hours and in the ointment base for six hours (in the conjunctival sac). The frequency of treatments was regulated according to the requirements of the patient. Frequent applications are not necessary. There are definite indications for its use in management of the following conditions: blepharitis, acute conjunctivitis, corneal ulcer, dacryocystitis, stye and ocular injuries and in post-operative routine. There are indications for chronic conjunctivitis, infected socket and involvement of other external structures with possible secondary infection.

The author states that it is difficult to assess the value of the drug in cases of injury, as experience is insufficient, nor can anything be said at present regarding its value in the prevention of recurrence of inflammation. Penicillin, being bacteriostatic and not bactericidal, will have little power to prevent recurrences unless it can be used more or less as a routine in intervals between exacerbations. It is important that all patients having facial burns with ocular involvement be given penicillin from the very beginning of treatment. The author believes that by following this procedure a number of ulcers due to exposure keratitis can be avoided.

The concentration of 100 Oxford units per gram of ointment is in contrast to that of 600 to 800 Oxford units per gram used by Florey and of more than 1,000 Oxford units in the ointment made by Dr K Meyer (von Sallmann, L., and Meyer, K. Penetration of Penicillin into the Eye, ARCH OPHTH 31: 1 [Jan] 1944).

ARNOLD KNAPP

Toxic Amblyopia

ACTION OF ANTIFREEZE ON THE VISUAL ORGAN A P ASTAKHOVA, Vestnik oftal 22: 33, 1943

Antifreeze is a mixture of 55 per cent of ethylene glycol and water. The alcohol has two carbon atoms, it is colorless, odorless, slightly sweet, easily diluted in water and liquid. A dose of 200 cc is sufficient to cause death. Astakhova examined 30 patients, 13 of whom died within the first day after exposure because of paralysis of cardiovascular and motor centers. In 6 of these patients the retina was cyanotic. One patient had optic neuritis, with decrease of visual acuity to ability to count fingers and a central scotoma in each eye, another patient had pallor of the optic disks, and 5 had hyperemia of the retinal blood vessels. The action of the antifreeze on the eye can be explained by its content of methyl alcohol.

O SITCHEVSKA

Society Transactions

EDITED BY DR W L BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H JOHNSON, M D , Chairman

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Feb 19, 1945

Traumatic Injuries of the Eyes in Soldiers

DR BENJAMIN RONES and MRS HELENOR WILDER, Washington, D C

The authors studied 399 eyes removed from soldiers because of injuries in training and combat and sent to the Army Institute of Pathology, Washington, D C This series consisted of 373 eyes with penetrating wounds and 26 eyes with contusion injuries Although 57 eyes were found to contain metallic foreign bodies, it was noteworthy that only 3 showed siderosis bulbi Examination of the enucleated globes revealed a wide variety of tissue injuries and of mechanisms of repair The penetrating wounds resulted in prolapse and incarceration of all the intraocular structures, separately and in combinations Intraocular hemorrhages constituted the commonest finding They were seen in all the tissues, in various stages of resorption and organization The most frequent single structural change was traumatic cataract Inflammatory changes in various stages were common Secondary glaucoma was the most frequent sequel of contusion injuries, while phthisis bulbi occurred more often after penetrating wounds The absence of any case of sympathetic ophthalmia was worthy of emphasis

DISCUSSION

DR HAROLD HENRY JOY, Syracuse, N Y As I recall, there were no cases of sympathetic ophthalmia in the American Army in World War I, and I believe none in the British Army

DR ARNOLD KNAPP I should like to compliment Dr Rones and Mrs Wilder on this splendid piece of work Only one thing strikes me as difficult in this investigation—that is, to decide on the principal injury in these severely damaged eyes which had to be enucleated and to determine the order in which the other changes occurred

DR ELBERT S SHERMAN, Newark, N J If I understood Dr Rones correctly, siderosis bulbi was observed in only 3 of the 57 eyes with retained intraocular foreign bodies, most of them metallic

He said nothing about the interval between the date of injury and the enucleation As siderosis

is seldom apparent clinically earlier than five months after the injury, there should have been, unless most of these eyes were enucleated early, more instances of siderosis

DR BENJAMIN RONES, Washington, D C Dr Joy is correct in stating that there were no cases of sympathetic ophthalmia in the United States Army or the British Army after World War I That does not detract from the credit due American ophthalmologists in the present war, for it is known that results in civilian practice are not so good Military surgeons obviously have more latitude than civilian surgeons about removing eyes, and their percentage of cases of sympathetic ophthalmia has been zero

Dr Knapp is correct There is not a great deal we can do with this material, and it is difficult to know how far we dare go in drawing conclusions We are trying to find out what we can do and what we cannot do We can describe our pathologic findings We cannot always depend on the clinical history that is given us, but we are trying by follow-up studies to get as much as we can from the field surgeons We have been fortunate that until recently Colonel Vail was consultant in ophthalmology for the European theater, and he insisted that information concerning time intervals and descriptions of the injuries should accompany the specimens Although our primary interest is in the pathologic findings, it is to our advantage to have as complete a clinical record as possible

Concerning the question of siderosis, one must bear in mind that the majority of the 57 eyes were removed shortly after injury In the next paper we shall present a more detailed study of intraocular foreign bodies At present, I cannot give the interval between injury and enucleation for the eyes that were retained for any length of time The majority of the eyes were taken out shortly after injury because they were so badly damaged that it was not worth attempting removal of the foreign body We shall know later how many cases of siderosis occurred after late retention of foreign bodies

Surgical Procedures on the Anophthalmic Orbit. CAPT ARTHUR GERARD DE VOE (MC), U S N R

A review of the difficulties encountered in fitting artificial eyes revealed that depression of the upper lid and loss of the orbital fold are commonly encountered Reasons for this occurrence were hypothesized, and methods of treatment were described

Implantation of cartilage subperiosteally in the floor of the orbit can be employed in cases of depressed fracture of the floor. Dermal grafts to the upper lid are useful in obliterating the depression when no fracture is present.

Another common defect is flaccidity of the lower lid and loss of the inferior fornix. This can be remedied by construction of a new fornix, lined, if necessary, with mucous membrane from the lid. This procedure was illustrated with a motion picture.

DISCUSSION

DR WENDELL L HUGHES For correction of the depressed upper lid, there has been developed in the United States Naval Hospital at Bethesda, Md., a prosthesis with a thickened ridge along its upper edge. I wonder whether Captain De Voe has had any experience with it. In cases in which there is a definite fracture of the floor of the orbit, the procedure that Captain De Voe mentioned, in which cartilage is placed in the floor of the orbit, closing the hole in the floor and adding tissue to the orbit, gives as satisfactory a result as can be obtained. I was much interested in the use of a mucous membrane graft when there is a shallow lower fornix. It is an excellent procedure, and one which I shall try in the near future. I should like to report the case of a girl of 18 years who had had an artificial eye ever since she was a youngster. The artificial eye did the thing which Captain De Voe showed in his moving pictures, that is, it slipped out over the lower lid. In this case the conjunctiva was of sufficient extent that it could be dissected free and redistributed, to form a fornix below. There is usually one place in the middle of the socket where the conjunctiva is firmly adherent to the underlying structures. After it is freed double-armed sutures can be used to bring down and retain the fornix. There was sufficient conjunctiva in this case so that no additional tissue was needed.

Captain De Voe's comment on the use of a combination of skin and mucous membrane in the orbit is apropos. The two do not mix well.

In a case like that of Captain De Voe's in which he had difficulty in putting in the artificial eye, I think a flexible prosthesis would do nicely. A concavoconvex one can be cut from a rubber ball. It has an advantage over the flat prosthesis which is prepared from rigid plastic material.

CAPT ARTHUR GERARD DE VOE I have tried using a thickened ridge along the upper edge of the prosthesis and have had no success; the device merely widens the eye and makes the sclera stand out, without improving the appearance.

Ocular Manifestations Due to Nutritional Deficiencies in Naval Personnel in the Southwest Pacific **ARTHUR A KNAPP (MC), U S N R**

The patients considered in this report were Naval personnel at battle stations for six to eighteen months. Canned food had been used

almost exclusively and deficiency in several essential elements, among them vitamins and minerals, was unavoidable.

Except for the chorioretinitis, each of the disease entities discussed—myopia, night blindness, vernal catarrh, or allergic conjunctivitis, haziness of the fundus oculi, pallor of the optic nerve, and retrobulbar neuritis—has been shown to have a dietary background, but the extent to which a deficient diet is an etiologic factor has not been thoroughly studied. It is possible that in these conditions the food intake does not account for the entire picture.

The subjects exhibiting vernal catarrh, chorioretinitis and disease of the optic nerve responded well and quickly to the new diet when undernourishment was the primary cause. They showed improvement within a few days. The progress of the myopic patients could not be followed over a sufficiently long period. Ample studies, however, already have been made to establish the need of proper nutrition in cases of myopia.

Common to all of these patients is the fact that, except for the ocular manifestations, they did not reveal any clinical signs or symptoms of nutritional deficiency in other parts of the body. The men all appeared healthy, that is, the systemic nutritional lack was in a latent state. The ocular signs were the sole revealing indications of the underlying metabolic disorder.

A similar situation prevailed in much of our research work with animals. Often the pathologic condition of the eyes was the only clinical clue to the deficiency status.

Actually, the diets served at the base hospital, situated in a fine food-producing country in the Southwest Pacific, were far superior to those received by the men at their battle stations. Particular attention was paid to the milk intake. A quart (1,000 cc) was advised, to give the necessary gram of available calcium. In addition, the diets frequently were fortified with vitamins A, B, C and D. The vitamin D intake especially was stressed, for lack of it, apparently, may give rise to many and diverse pathologic changes in the eyes.

Certain ocular changes were demonstrated in these patients with a faulty food intake—axial myopia, vernal catarrh or allergic conjunctivitis, a slightly hazy fundus oculi, and disease of the optic nerve. These several signs of ocular disease in this series further corroborate the results of earlier research on animals and human subjects.

Evidently, a lack of vitamin D and/or calcium is a potent cause of disease of the eyes.

It is recommended that, aside from any other therapy, comparatively large doses of vitamin D and calcium be prescribed in all cases of progressive axial myopia, vernal catarrh and night blindness.

DISCUSSION

DR GILBERT DAULDORF, Valhalla, N Y. Dr Knapp's work is stimulating, original and highly

commendable, particularly since he found an effective method of treating what must have been a common disorder. It would be pretentious of me to comment on the way in which his report fits into knowledge of diseases of the eye. I can comment on how it is correlated with what is known of nutrition. It is obvious that Dr Knapp takes into consideration these principles, for he has qualified the significance of the diet in deficiency diseases. It is recognized that nutritional deficiency does not necessarily mean a deficient diet, that symptoms and lesions due to deficiency can develop with a diet which is adequate for the average man. There is nothing mysterious about that. A man with bacillary dysentery who has an average fluid intake will become dehydrated, and a man in an advanced stage of cancer will become cachectic even though he is getting a normal diet. In both cases the patient becomes deficient in vitamins as well as dehydrated or cachectic. In these cases the explanation is relatively simple, in others it is complicated. The service men Dr Knapp spoke of presumably were receiving a different diet while in combat, an emergency ration which it may be assumed, was adequate in vitamins and minerals. But they were placed on it rather suddenly, and at the same time they were exposed to a different environment and to the stresses of warfare. Such conditions may influence the relative adequacy of the diet.

Little is known about the adult's requirement of vitamin D. Hepatic disease, the ingestion of certain metals, the acid-base nature of the diet and the vitamin E content, all influence the requirements of vitamin D. Perhaps climate does, also. I recall a study by Dr Mills in which rats adapted to a high humidity and temperature—to tropical conditions—were found to require twice as much vitamin K as before.

The suddenness of change in diet may upset nutritional balances. It seems probable that man, like many other animals, can adapt to different levels of nutrition if given time. This is a lively subject in vitamin nutrition, which in some ways goes back twenty years to the observation that rats given a thiamine-deficient diet occasionally are able to adapt to the deficiency. Certain animals fared well, while their mates wasted away and died. The phenomenon was called refection. It is now known that some men can do the same thing. They synthesize the thiamine they need. This is dependent on the proper bacterial flora, which depends, also, on other factors in the diet which encourage the thiamine-synthesizing flora.

Environment is of considerable importance in nutrition. The importance of organic disease and of functional disturbances is greater. Most of the cases of deficiency disease occurring in North America are secondary to some other condition. I suspect that something of this kind operated among Dr Knapp's patients. Secondary lesions in deficiency states respond to vitamin therapy,

but they are cured only by correction of the underlying cause. In how many cases the underlying cause was corrected by bringing these service men back to a base hospital one does not know.

May I add one other observation? The reason that one must speculate about these things and the reason that Dr Knapp cannot be certain of the part which vitamin D played in the ocular lesions he noted is simply that objective, reliable criteria for minor degrees of vitamin deficiency do not exist. Nutritionists have failed to develop means of identifying these conditions. Ophthalmologists have contributed some of the best tests, such as the estimation of regeneration of visual purple, and I hope that they will devise others. Dr Knapp's results suggest that this may occur.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

WARREN S REESE, M.D., *Chairman*

GEORGE F J KELLY, M.D., *Clerk*

March 15, 1945

Traumatic Iridodialysis: Its Surgical Correction, with Report of a Case. DR A BARLOW and DR HERMAN L WEINER (by invitation)

This paper will be published in full, with discussion, in a future issue of the ARCHIVES.

Symmetric Defects of the Lower Lids Associated with Abnormalities of the Zygomatic Processes of the Temporal Bones. DR IRVING H LEOPOLD and (by invitation) DR FRANCIS MAHONEY and MISS MABEL L PRICE

This paper will be published in full, with discussion, in a future issue of the ARCHIVES.

Intravitreal Penetration of Penicillin and Penicillin Therapy of Infections of the Vitreous DR IRVING H LEOPOLD

This paper was published in the March 1945 issue of the ARCHIVES, page 211.

DISCUSSION

DR W ZENTMAYER Rycroft recently reported the results obtained with penicillin by the ophthalmologists in the British North African and Central Mediterranean forces (*Brit J Ophth* 29: 57 [Feb] 1945). The study is largely clinical, and this may explain the apparent disagreement between their results and those reported by Dr Leopold. They found that penicillin does not enter the ocular media when given intramuscularly. Such a method of administration does not influence the course of deep infections of the eye.

The eye will tolerate large concentrations of penicillin when injected into the media, but such concentrations do not control deep infections

DR H MAXWELL LANGDON The organism with which these experiments were carried out was selected especially for its lack of resistance to penicillin. It would be interesting to know the effect on other organisms in the vitreous. The organisms resistant to penicillin, of course, have been fairly well recognized and classified, but, as I understand it, some are more readily affected than others. Without cultures, of course, these less resistant organisms cannot be identified, so in the ordinary clinical case therapy is bound to be a trial and error procedure.

DR IRVING H LEOPOLD I want to thank Dr Zentmayer and Dr Langdon for their discussions.

I too, found Colonel Rycroft's excellent article discouraging. In all of his cases of inflammation of the vitreous the condition was due to intravitreal penetration of a foreign body. In only 2 was there improvement, and in these cases the offending foreign body was removed. In no case did cultures of the aqueous or the vitreous reveal that the exciting inflammatory agent was a penicillin-sensitive organism.

In all of Rycroft's cases intravitreal injections of penicillin were not made until the inflammatory process had become well established. In the experiments on rabbit eyes, therapy was instituted two hours after inoculation of the vitreous with *Staphylococcus aureus*. Studies by von Sallmann, Meyer and Di Grandi (Experimental Study on Penicillin Treatment of Ectogenous Infection of Vitreous, *ARCH OPHTH* 32: 179 [Sept] 1944) indicate that little can be expected from direct intravitreal injection of penicillin later than twelve hours after inoculation with the penicillin-sensitive organism, but that excellent results may be obtained with earlier institution of therapy.

Rycroft's studies on human eyes showed, as did the experiments on rabbit eyes, that intra-

muscularly administered penicillin did not produce detectable levels of the drug in the vitreous of normal eyes. He could not detect penicillin in the vitreous of inflamed human eyes after intramuscular administration, whereas the vitreous of inflamed rabbit eyes did possess detectable but inadequate concentrations of penicillin.

It is known that the permeability of capillaries in the rabbit eye is greater than that of capillaries in the human eye in inflammatory states. For example, Brown and Nantz (*Am J Ophth* 27: 1220, 1944) pointed out that the rabbit's secondary aqueous contains considerable fibrin, whereas the secondary aqueous of the adult human eye shows little, if any, fibrin. This difference in permeability must be kept in mind in drawing analogies between the data accumulated by experiments on rabbit eyes and those derived from studies on human eyes.

Staph aureus was used in these studies because it was extremely sensitive to penicillin. The main purpose of the experiment was to compare the possible chances of controlling infections of the vitreous by the various methods of administration. I believe that the experimental data have shown the inadequacy of systemic therapy. Rycroft's experience would bear this out. The experimental studies indicate that direct intravitreal injections may be effective if one treats the infection early enough. The latter observation can be said to apply only when the infection of the vitreous is due to a penicillin-sensitive organism.

I agree with Dr Langdon that these experiments are only an introduction to the problem of treating infection of the vitreous and that much more laboratory and clinical work will be necessary before the ideal method of treating infections of the vitreous with penicillin is known.

Reevaluation of the Herbert Operation for Glaucoma DR LOUIS LEHRFELD

This paper will be published in full in a future issue of the ARCHIVES.

Obituaries

JOSEPH IMRE, M D

1884-1945

Imre was born of a long line of outstanding Protestant scholars, at Hódmezovásárhely, Hungary, on June 9, 1884. His father was in general practice and was later professor of ophthalmology at the University of Kolozsvár (Cluj), which position he had to leave when, at the end of World War I, Rumania took over Transylvania. After receiving his doctor's diploma at the University of Budapest, young Imre became assistant at the eye clinic of Prof E von Grósz. In 1911-1912 he spent a year at the Axenfeld clinic, in Freiburg, Germany, and in 1914 he became associate professor at his alma mater. As head of the department of ophthalmology of a military hospital during World War I, he had ample opportunity to do plastic operations. His artistic sense combined with surgical skill and imaginative power led to the perfection of the sliding flap technic in the reconstruction of defects of the lid, a method he inaugurated before 1914. The unequalled results of his plastic operations were published in several articles, as well as in an atlas (1930), and were reported in a paper delivered at the meeting of the Ophthalmological Society of the United Kingdom in 1937. In 1918 he was appointed professor at the Hungarian University of Pozsony, but the next year he had to leave his chair because this city (Bratislava) became part of Czechoslovakia. Imre faithfully followed the medical school on its odyssey to Budapest and finally to Pecs, in 1924. There he found an excellent atmosphere, and in the quietness of this small town, he and his assistants spent five years devoted to study and research. He was the first to point out the frequency of endocrine disturbances in patients with glaucoma and advocated the use of glandular preparations. Another of his original ideas was the discovery that microscopically thin, electrically distributed metal layers can be used as filters for certain visible and invisible rays and he had such glasses constructed.

But surgery was his favorite subject. As early as 1918 he systematically used the intracapsular extraction of cataract. In 1925 he performed this operation in nearly 50 per cent of cases and also removed the capsule afterward when it was torn.

In 1928-1929 he became rector of the University of Pecs and in 1929 head of the state

ophthalmologic hospital in Budapest. In the following years he was chiefly interested in the perfection of corneal transplantation and of the operation for retinal detachment. On the latter subject he read a paper before the Chicago Ophthalmological Society. He also modernized a textbook of ophthalmology. The one hundred and eighty bed hospital and a large practice would have been a real burden to anybody, but



JOSEPH IMRE, M D

1884-1945

Imre saw far beyond the limits of his profession, as the representative of Hungarian ophthalmology abroad, as a founder and regional chairman of the Rotary Association and with friends all over the world, it was his duty, he felt, to call attention to the problems and tragedy of his country.

In 1939 Imre was appointed head of the eye clinic of the University of Budapest. The Nazi-minded professors made his life bitter because of his international connections and liberal political views. Even his passport was taken away so that he could not leave the country.

The shortsighted policy of its leaders swept Hungary gradually closer to Nazism, away from the Anglo-Saxon democratic world, which Imre loved so much. He saw the impending tragedy to his country. His patriotic heart first broke in the fall of 1941 and stopped beating when the final collapse came, in January 1945.

A fascinating teacher and a most stimulating guide to his assistants, Imre was a charming man in social life, an enthusiast in regard to

betterment of the world, a violinist and an artist, as so many great physicians are.

He is survived by his widow, a son, who is a physician, and a married daughter. Hungary has lost one of the very few men who had the talent, education, liberal ideals and international connections—in a word, the qualities—which could have made him a well qualified leader in this dire hour of his country.

ANDREW DE ROETTH

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

Summer Graduate Course in Ophthalmology, University of Rochester School of Medicine and Dentistry—The thirteenth summer graduate course in ophthalmology of the University of Rochester School of Medicine and Dentistry, Rochester, N Y, will be held July 30 to Aug 2, 1945.

The following lectures have been announced:

Monday, July 30 "Cataract Surgery," Dr D B Kirby, "Toxoplasmosis" and "Recent Advances in Orbital Roentgenography," Dr Raymond L Pfeiffer, and "Ophthalmic Lenses." Mr Scott Sterling. In the evening there will be a symposium on "Industrial Ophthalmology," conducted by Dr A C Snell, Dr Joseph Tiffin and Dr A Snell Jr.

Tuesday, July 31 "Visual Field Changes Produced by Intracranial Lesions" and "Vascular Affections of the Eyes and Cerebral Visual Structures," Dr Donald J Lyle, "Medical Ophthalmology" and "Surgical Treatment of Strabismus," Dr Glen G Gibson and "Physiological Optics in Refraction," Mr Fred Jobe.

Wednesday, August 1 "Treatment of Glaucoma" Dr Paul A Chandler, "Surgical Pathology of Glaucoma and Cataract" and "Malignant Melanoma and Other Conditions Which May Produce Glaucoma," Dr T L Terry, and "Everyday Spectacle Problems," Mr Irving Lueck.

Thursday morning, August 2 will be devoted to the surgical clinic at the Strong Memorial Hospital.

Applications for registration should be mailed to Dr John F Gipner, Strong Memorial Hos-

pital, Rochester 7, N Y. The tuition charge for the course will be \$40.

Annual de Schweinitz Lecture—Col Derrick T Vail will deliver the annual de Schweinitz Lecture before the College of Physicians, Philadelphia, Section on Ophthalmology, on Nov 15, 1945.

UNIVERSITY NEWS

Honorary Degree Awarded to Dr Hermann M Burian by Colby College—On June 3, 1945, Colby College, Waterville, Maine, awarded the honorary degree of Doctor of Science to Hermann M Burian, M D, ophthalmologist in chief, Dartmouth Eye Institute, Hanover, N H. The citation of Colby College read as follows:

Hermann Martin Burian, son of a well-known professor of physiology, student of languages, literature, and music, as well as science educated in the most renowned laboratories of the old world, you have won a distinguished place in the new. In the field of ocular motility and binocular vision your work has received the praise of those of your colleagues whose judgment is most to be esteemed and you are already hailed as one of the builders of American ophthalmology.

University of Oregon Medical School—Dr Frederick A Kiehle has resigned as professor and head of the department of ophthalmology, after many years of distinguished service to the university of Oregon medical school. Dr Kiehle has been appointed professor emeritus, and Dr Kenneth C Swan has been appointed professor and head of the department of ophthalmology.

Directory of Ophthalmologic Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Bailliart, 66 Boulevard Saint-Michel, Paris, 6^e, France
Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ostflandern, Belgium
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6^e, France

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INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

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Secretary Dr Frederick Ridley, 12 Wimpole St, London, W 1

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Secretary Dr K S Sun
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Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

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Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping
Place Peiping Union Medical College, Peiping Time Last Friday of each month

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

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All correspondence should be addressed to the Assistant Secretary

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Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England
Place Birmingham and Midland Eye Hospital

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Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo
All correspondence should be addressed to the secretary, Dr Mohammed Khalil

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Secretary Dr H D Dastur, Dadar, Bombay 14, India
Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

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Place Edinburgh and Glasgow, in rotation

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ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159,
Rosario
Secretary Dr Arturo Etchemendigaray, Villa Constitucion, Santa Fe
Place Rosario Time Last Saturday of every month,
April to November All correspondence should be
addressed to the President

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apolis

In compliance with the request of the Office of Defense
Transportation and in the interest of the national war
effort a meeting will not be held in 1945

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Secretary-Treasurer Dr Harold H Heuser, 207
Davidson Bldg, Bay City, Mich
Place Saginaw or Bay City, Mich Time Second
Tuesday of each month, except July, August and
September

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EAR, NOSE AND THROAT**

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Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan
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Time Last Thursday of September, October, November,
March, April and May

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Rock

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President Dr C A Ringle, 912-9th Ave, Greeley
Secretary Dr W A Ohmart, 1102 Republic Bldg,
Denver
Place University Club, Denver Time 7 30 p m,
third Saturday of each month, October to May, in-
clusive

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Secretary-Treasurer Dr W H Turnley, 1 Atlantic
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OTOLARYNGOLOGY**

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Secretary Dr William A Kennedy, 372 St Peter St,
St Paul
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May

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Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg,
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Secretary-Treasurer Dr Lewis Jordon, 1020 S W
Taylor St, Portland
Place Good Samaritan Hospital, Portland Time
Third Tuesday of each month

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AND OTOLARYNGOLOGY**

President Dr Lewis T Buckman, 83 S Franklin St,
Wilkes-Barre
Secretary Pro Tem Dr Paul C Craig, 232 N 5th
St, Reading
Time Last week in April

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OTOLOGICAL SOCIETY**

Acting President Dr N Darrell Harvey, 112 Water-
man St, Providence
Secretary-Treasurer Dr Linley C Happ, 124 Water-
man St, Providence
Place Rhode Island Medical Society, Library, Prov-
idence Time 8:30 p m, second Thursday in
October, December, February and April

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AND OTOLARYNGOLOGY**

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Place University Club, Salt Lake City Time 7:00
p m, third Monday of each month

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DIRECTORY

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OTOLARYNGOLOGY

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Secretary-Treasurer Dr V C Malloy, 2d National
Bank Bldg, Akron, Ohio
Time First Monday in January, March, May and
November

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President Dr B M Cline, 153 Peachtree St N E,
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Acting Secretary Dr A V Hallum, 478 Peachtree
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Place Grady Hospital Time 6 00 p m, fourth Mon-
day of each month, from October to May

BALTIMORE MEDICAL SOCIETY, SECTION ON
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Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,
Baltimore
Secretary Dr Thomas R O'Rourk, 104 W Madison
St, Baltimore
Place Medical and Chirurgical Faculty, 1211 Cathedral
St Time 8 30 p m, fourth Thursday of each
month from October to March

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President Each member, in alphabetical order
Secretary Dr Luther E Wilson, 919 Woodward Bldg,
Birmingham, Ala
Place Tutwiler Hotel Time 6 30 p m, second
Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr Michael J Buonaguro, 589 Lorimer St,
Brooklyn
Secretary-Treasurer Dr Benjamin C Rosenthal, 140
New York Ave, Brooklyn 16
Place Kings County Medical Society Bldg, 1313 Bed-
ford Ave Time Third Thursday in February, April,
May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave,
Buffalo
Secretary-Treasurer Dr Sheldon B Freeman, 196
Linwood Ave, Buffalo
Time Second Thursday of each month

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OTOLARYNGOLOGY

President Each member, in alphabetical order
Secretary Dr Douglas Chamberlain, Chattanooga
Bank Bldg, Chattanooga, Tenn
Place Mountain City Club Time Second Thursday
of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr Samuel J Meyer, 58 E Washington
St, Chicago 2
Secretary Dr W A Mann, 30 N Michigan Ave,
Chicago 2
Place Continental Hotel, 505 N Michigan Ave
Time Third Monday of each month from October
to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY
STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati
Secretary Dr A A Levin, 441 Vine St, Cincinnati
Place Cincinnati General Hospital Time 7 45 p m,
third Friday of each month except June, July and
August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr M Paul Motto, Rose Bldg, Cleveland
Secretary Dr H H Wygand, Guardian Bldg, Cleve-
land
Time Second Tuesday in October, December, February
and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION
ON OPHTHALMOLOGY

Chairman Dr W S Reese, 1901 Walnut St,
Philadelphia
Clerk Dr George F J Kelly, 37 S 20th St,
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to April, inclusive

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Chairman Dr Erwin W Troutman, 21 E State St,
Columbus, Ohio
Secretary-Treasurer Dr T Rees Williams, 380 E
Town St, Columbus 15, Ohio
Place University Club Time 6 15 p m, first Mon-
day of each month, from October to May, inclusive

CORPUS CHRISTI EYE, EAR, NOSE AND
THROAT SOCIETY

Chairman Dr C B Collins, 704 Medical Professional
Bldg, Corpus Christi, Texas
Secretary Dr L W O Janssen, 710 Medical Profes-
sional Bldg, Corpus Christi, Texas
Time 6 30 p m, third Tuesday of each month from
October to May

DALLAS ACADEMY OF OPHTHALMOLOGY AND
OTO-LARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg,
Dallas 1, Texas
Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,
Texas
Place Dallas Athletic Club Time 6 30 p m, first
Tuesday of each month from October to June The
November, January and March meetings are devoted
to clinical work

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa
 Time 7 45 p m, third Monday of every month from September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically
 Secretary Dr Cecil W Lepard, 1025 David Whitney Bldg, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time First Wednesday of each month, November to April, inclusive

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Raymond S Goux, 545 David Whitney Bldg, Detroit 26
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

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President Appointed at each meeting
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany
 Time Third Wednesday in October, November, March, April, May and June

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President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Dennis Smith, 623 Security Bldg, Long Beach 2, Calif
 Secretary-Treasurer Dr Robert Null, 710 Security Bldg, Long Beach 2, Calif
 Place Seaside Hospital Time Last Wednesday of each month from October to May

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President Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif
 Secretary-Treasurer Dr K. C Brandenburg, 110 Pine Ave, Long Beach 2, Calif
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

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Chairman Each member in alphabetical order
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

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 Secretary Dr Frazier Williams, 1801 I St N W, Washington
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee
 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2
 Place University Club Time 6 30 p m, fourth Tuesday of each month from October to May

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Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada
 Time Second Thursday of October, December, February and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

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President Dr William H Ryder, 185 Church St, New Haven, Conn
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

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 Secretary Dr Wendell L Hughes, 131 Fulton Ave, Hempstead, N Y
 Time 8 30 p m, third Monday of every month from October to May, inclusive

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President Dr Maurice L Wieselthier, 117 E 30th St, New York
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York 28
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday of each month from October to May, inclusive

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President Dr James P Luton, 117 N Broadway, Oklahoma City
 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City
 Place University Hospital Time Second Tuesday of each month from September to May

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President Dr D D Stonecypher, Nebraska City, Neb
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

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President DR Thomas Sanfacon, 340 Park Ave, Paterson, N J
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia
 Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia
 Time First Thursday of each month from October to May

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President Dr George H Shuman, 351-5th Ave, Pittsburgh
 Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Isaac B High, 326 N 5th St, Reading, Pa
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

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President Dr Luther C Brawner, Professional Bldg, Richmond, Va
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va
 Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

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President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr Vincent Jones, 634 N Grand Blvd, St Louis
 Secretary Dr T E Sanders, 508 N Grand Blvd, St Louis 3
 Place Oscar Johnson Institute Time Fourth Friday of each month from October to April, inclusive, except December, at 8 00 p m

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President Dr Belvin Pritchett, 705 E Houston St,
San Antonio 5, Texas
Secretary-Treasurer Lt Col John L Matthews, AAF
School of Aviation Medicine, Randolph Field, Texas
Place San Antonio, Brooke General Hospital, Ran-
dolph Field or San Antonio Aviation Cadet Center
Time 7 p m, second Tuesday of each month from
October to May

**SAN FRANCISCO COUNTY MEDICAL SOCIETY,
SECTION ON EYE, EAR, NOSE AND THROAT**

Chairman Dr Roy H Parkinson, 870 Market St,
San Francisco
Secretary Dr A G Rawlins, 384 Post St, San
Francisco
Place Society's Bldg, 2180 Washington St, San Fran-
cisco Time Fourth Tuesday of every month except
June, July and December

**SHREVEPORT EYE, EAR, NOSE AND
THROAT SOCIETY**

President Dr David C Swearingen, Slattery Bldg,
Shreveport, La
Secretary-Treasurer Dr Kenneth Jones, Medical Arts
Bldg, Shreveport, La
Place Shreveport Charity Hospital Time 7 30 p m,
first Monday of every month except July, August
and September

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OTO-LARYNGOLOGY**

President Dr Clarence A Veasey Sr, 421 W River-
side Ave, Spokane, Wash
Secretary Dr Clarence A Veasey Jr, 421 W River-
side Ave, Spokane, Wash
Place Spokane Medical Library Time 8 p m, fourth
Tuesday of each month except June, July and August

**SYRACUSE EYE, EAR, NOSE AND
THROAT SOCIETY**

President Dr A H Rubenstein, 713 E Genesee St,
Syracuse, N Y
Secretary-Treasurer Dr I H Blasdell, 713 E
Genesee St, Syracuse, N Y
Place University Club Time First Tuesday of each
month except June, July and August

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THROAT SOCIETY**

Chairman Dr L C Ravin, 316 Michigan St, Toledo 2,
Ohio
Secretary Dr W W Randolph, 1838 Parkwood Ave,
Toledo, Ohio
Place Toledo Club Time Each month except June,
July and August

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Toronto, Canada
Secretary Dr W T Gratton, 216 Medical Arts Bldg,
Toronto, Canada
Place Academy of Medicine, 13 Queens Park Time
First Monday of each month, November to April

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President Dr Harold M Downey, 1740 M St N W,
Washington, D C
Secretary-Treasurer Dr Richard W Wilkinson, 1408
L St N W, Washington, D C
Place Medical Society of District of Columbia Bldg,
1718 M St N W, Washington, D C Time 7 30
p m, first Monday in November, January, March
and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn
Secretary Dr Samuel T Buckman, 70 S Franklin
St, Wilkes-Barre, Pa
Place Office of chairman Time Last Tuesday of
each month from October to May

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SIZE OF LATERAL FIELD THROUGH BIFOCALS

We have been asked quite often for information as to the width of the lateral field that is obtained through the segments of the various bifocals. We considered this a good question, for certainly some data on the subject should be on hand when prescribing bifocals—especially if vocational bifocals are being prescribed. In working out the answer to the question, two variables were found, first, of course, the diameter of the bifocal segment, and second the vertex distance, i.e. the distance from corneal vertex to lens.

The table below gives the width of the lateral fields for the four most commonly prescribed types of bifocals. The 20 m/m column is for the small segment bifocals, the 22 m/m for Ultex "B" or Kryptok, the 32 m/m for Ultex "E" and the 36 m/m for Ultex "A".

Aberrations create an unusable area of approximately one millimeter at the periphery of the segments and the table is therefore, calculated so as not to include this area.

DIAMETER OF SEGMENTS

VERTEX DISTANCE	20 m/m	22 m/m	32 m/m	36 m/m
8 m/m	28.0 in	30.0 in	37.5 in	43.0 in
10 m/m	22.5 in	24.0 in	30 in	36.0 in
12 m/m	18.5 in	20.0 in	25 in	30.0 in
14 m/m	16.0 in	17.0 in	21 in	26.0 in

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A study of the above table shows that the vertex distance has a tremendous effect on the size of the lateral field. For example, a 22 m/m segment at 8 m/m from the eye has the same lateral field as a 36 m/m segment at 12 m/m from the eye. If it were not for the fact that to a large extent the vertex distance is determined by the facial structure of the patient, it would be simple to fit every patient at 7 or 8 m/m and assure an adequate field for every case. However, facial structure does determine the vertex distance and so we feel the table will be useful.

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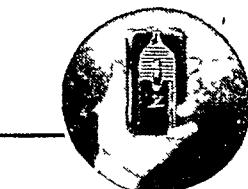
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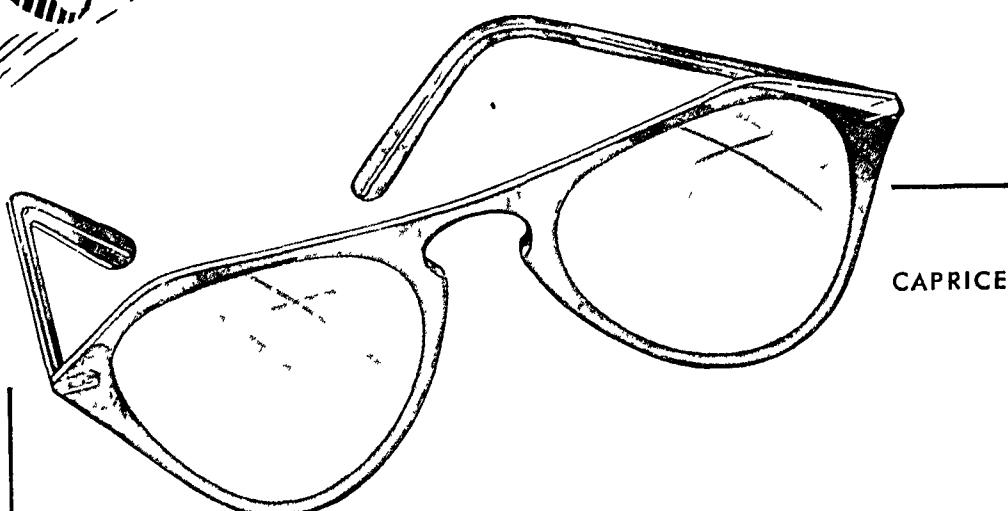
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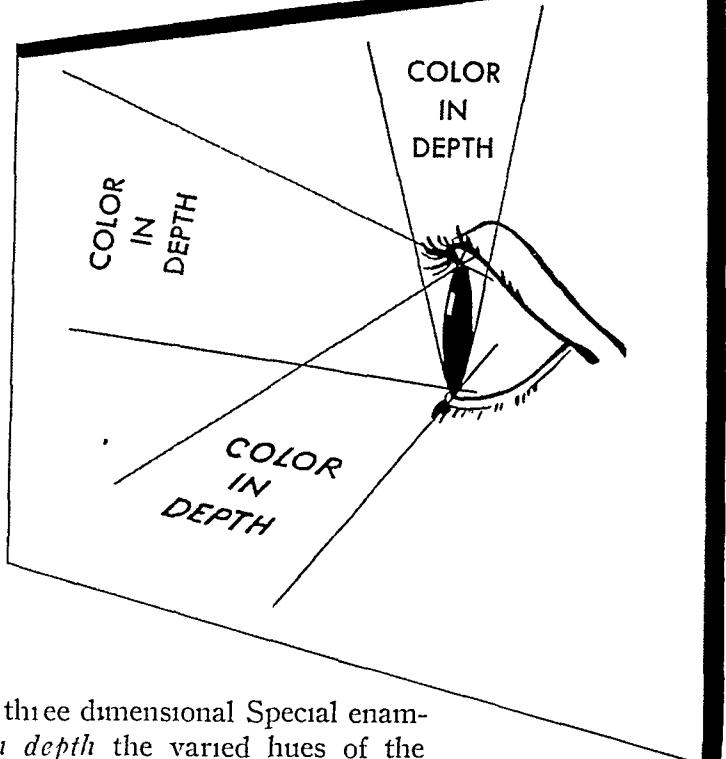
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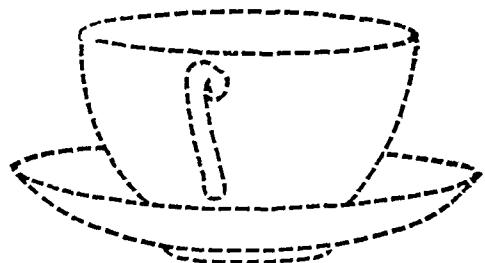
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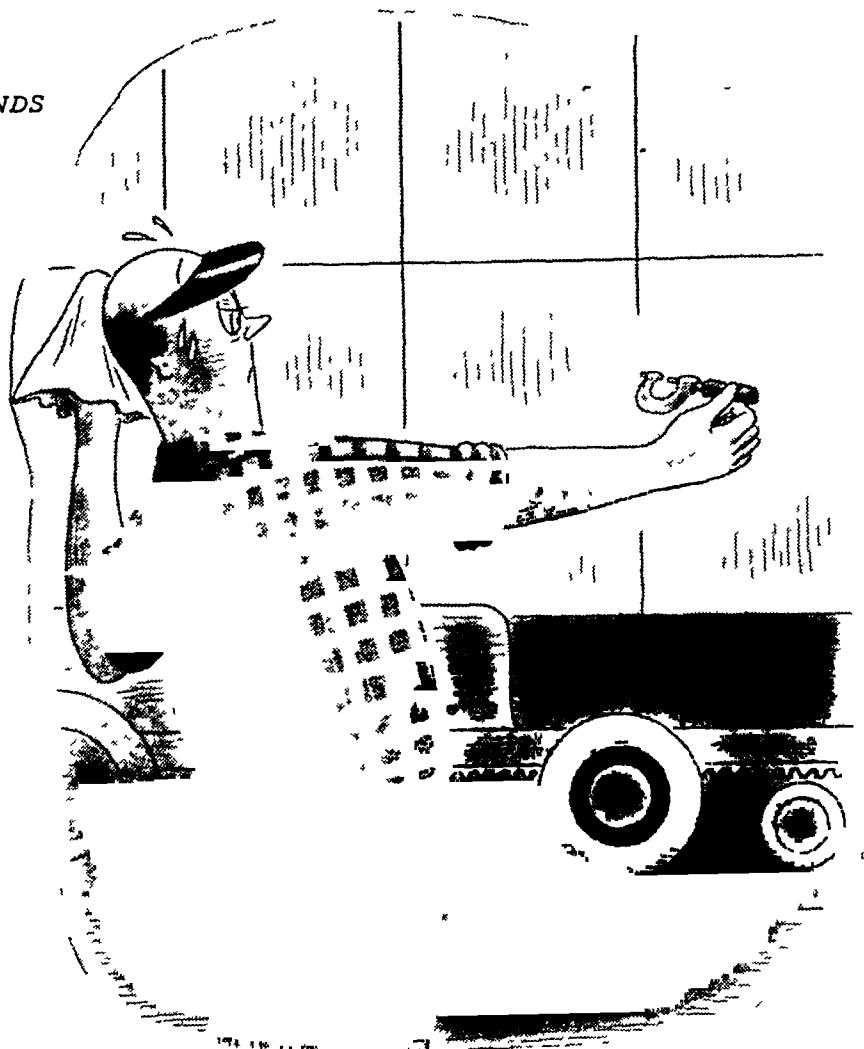
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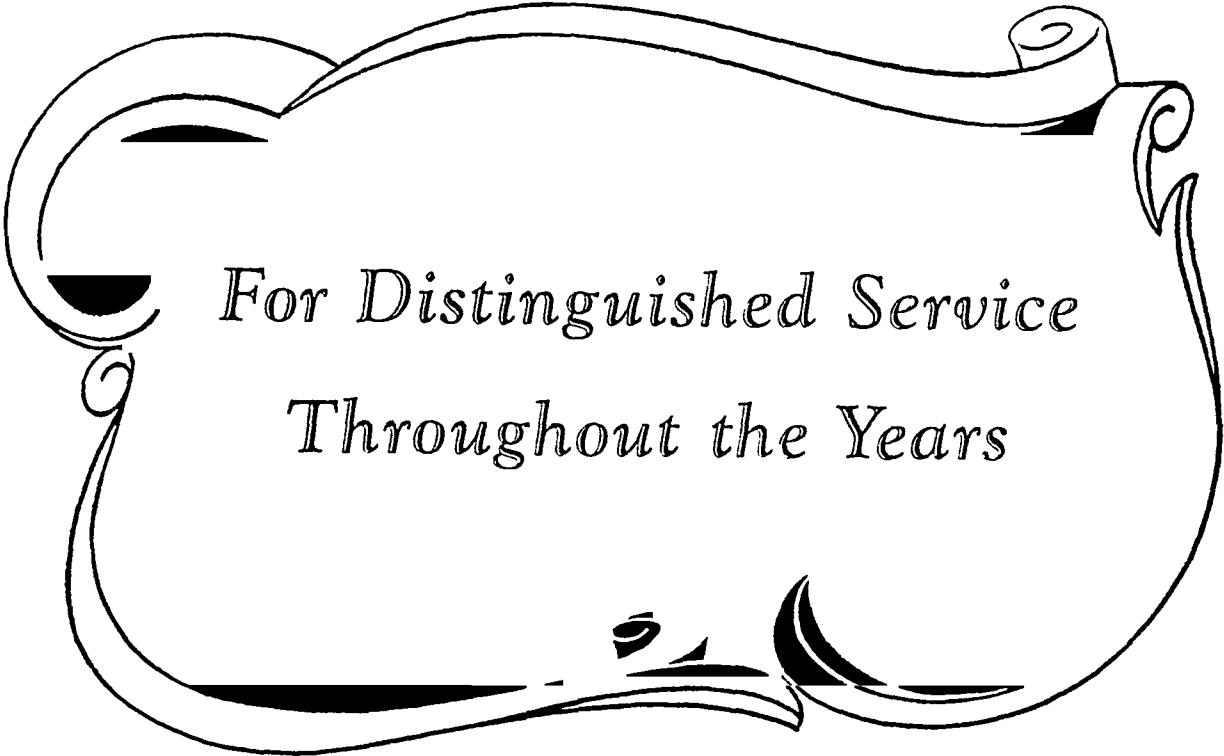
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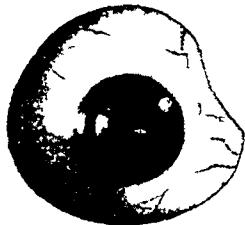


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VOLUME 33 (old series Volume 90)

JANUARY 1945

NUMBER 1

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ELEMENTARY ILLUMINATION FOR THE OPHTHALMOLOGIST

LEGRAND H HARDY, MD, AND GERTRUDE RAND, PHD
NEW YORK

Poor illumination produces ocular symptoms. The ophthalmologist is frequently consulted with regard to these symptoms, and he should be able to recognize and treat them effectively. He should, in addition be prepared to do his part in preventing, as well as in ameliorating, conditions which might cause such symptoms.

The scope of such activities may vary from simple, obvious advice to full scale cooperation with the illuminating engineer, the architect and the decorator. With his understanding of individual differences and needs, his freedom from commercial bias and his awareness of the part played by good lighting in the comfort and welfare of the eyes, the ophthalmologist occupies an important position in this phase of public health service. The purpose of this brief report is to outline the basic facts and principles of good lighting so that the ophthalmologist may be well guided in his individual or cooperative efforts to alleviate or avoid distress arising from defective illumination.

LIGHTING TERMS AND UNITS

The ophthalmologist is not concerned with the rigid mathematical and operational expressions used by radiation engineers. To him lighting is the science of creating and distributing light, which he describes as radiant energy evaluated according to its capacity to produce visual sensation. Since all practical sources of light include neighboring bands of radiations (infra-red or ultra-violet), these portions of the spectrum are included in his considerations as coincidental factors and are evaluated physiologically. Light (a temporal concept) and illumination (an areal concept) are not differentiated. One may overlook this lack of rigor, without condoning the meaningless phrase "foot candle power," so often encountered in ophthalmologic writings.

It will greatly facilitate the problem for the ophthalmologist if he will adopt three simple concepts:

From the Knapp Memorial Laboratories, Institute of Ophthalmology

1 Source—The source of light is evaluated in terms of power of which the candle (c) is the unit.

Illumination—The illumination at the working plane is evaluated chiefly with reference to the distance of the working plane from the source.

3 Brightness—This term, again a power term, may refer to the source itself (intrinsic brilliance, expressed as candles per square centimeter or per square inch or per square foot) or to light reflected toward the eye from an object.

Simple units to express measurements of these three factors may now be derived.

Source—The candle is the unit of luminous intensity. As a power term it expresses the intensity of the source. It is an antiquated concept, dating from the earliest attempts at evaluation and control of lighting. The old English sperm candle (six to a pound), which burned at the rate of 120 grains of spermaceti per hour, was taken as a standard. This standard has now been conserved by international standardizing laboratories in terms of incandescent lamps.

This candle flame emits luminous, or light, flux in all directions. The amount of this light flux encompassed in a unit solid angle (steradian) is the unit called a lumen. If the candle flame is condensed to a point and this point is situated at the center of a sphere with a radius of 1 foot, the amount of light falling on 1 square foot of the sphere is 1 lumen, and since the area of such a sphere is 4π square feet, there must be 4π , or 12.57 lumens, emitted by 1 candle.

Illumination—Illumination is the intensity of concentration of light falling on a particular surface, and one unit of measurement is the foot candle (ft c). The foot candle is defined as 1 lumen per square foot. In the example chosen, since every part of the sphere is 1 foot away from a source of 1 candle power, each square foot of the sphere receives 1 lumen, and the illumination is 1 foot candle.

If the surface were not spherical, but were a plane tangent to the sphere, the illumination

would be 1 foot candle only at one point on the plane, and it would be less than 1 foot candle on all other points, the intensity depending on the distance from the point source of 1 candle power and the angle of incidence.

It is thus seen that the illumination (which means intensity of light flux, and hence the phrase "intensity of illumination" is redundant) varies with three factors—the power of the source, the distance from the source and the angle of incidence. However, these three factors operate differently. It is worth remembering that the illumination varies directly with the power of the source, that is, if a 2 candle power lamp is substituted for a 1 candle power lamp, the illumination is doubled. This is a direct proportion.

The variation with distance is not direct; illumination is inversely proportional to the square of the distance from the source. This is the inverse square law, applicable to all radiation, and it means that in order to obtain the same illumination at 2 feet as at 1 foot the power of the source must be increased by 2², or, again, a 100 candle power lamp which gives an illumination of 100 foot candles at a distance of 1 foot gives at a distance of 2 feet only $\frac{100}{2^2}$, or 25, foot candles, at a distance of 5 feet $\frac{100}{5^2}$, or 4, foot candles and at a distance of 10 feet $\frac{100}{10^2}$, or 1, foot candle. This is an important consideration and is the chief reason for supplementing general room illumination with local fixtures. It should be noted in passing that the inverse square law applies rigidly only to point sources and practically is valid only for long distances when large sources are used. It is invalid when the distance is less than five times the dimension of the source. Thus, the illumination from large luminaires or from nearby tubular lamps needs to be measured, rather than calculated.

Finally, if the light does not strike the surface perpendicularly but is incident at an angle, the same amount of flux is distributed over a larger area, and the illumination consequently decreases. The amount of the decrease can readily be shown to be equal to the cosine of the angle of incidence. This is known as the cosine law.

Brightness.—It is obvious that only the light which enters the eye is useful for seeing and that unless one is looking at self-luminous objects this light must be reflected. The amount of light reflected from an object will vary with the amount of light incident on it and with its physical characteristics (reflectance). A white object with high reflectance will appear brighter

under a given illumination than a dark object with low reflectance. The ratio (percentage) of the amount of light reflected from an object to the amount of light incident on the object is a measure of its reflectance and determines its brightness.

The simplest expression of brightness in terms of the units we have derived is the apparent foot candle. If an object is illuminated with 100 foot candles and has a reflectance of 80 per cent, 80 of these 100 foot candles will be reflected back, and the object will have a brightness of 80 apparent foot candles. In England the term equivalent foot candles is used. Or brightness can be expressed in terms of lumens per square unit of area. If 1 lumen is emitted or reflected from each square centimeter, the area has a brightness of 1 lambert (L). This is very high brightness, and for most practical situations a smaller unit is desired. Such a unit is the millilambert (mL), or 0.001 lambert. If the unit area is taken as the square foot, a surface emitting or reflecting 1 lumen per square foot has a brightness of 1 foot lambert (ft L). Since there are 1,076 sq cm in 1 square foot, the foot lambert equals 1,076 millilamberts, that is, the foot lambert, the millilambert and the apparent foot candle, as expressions of brightness, are practically interchangeable.

A point which often puzzles the ophthalmologist is why the brightness of an object does not noticeably decrease as one recedes from it. We have frequently been asked, for example, what the illumination of a test chart is to a patient 20 feet (6 meters) away. It is a fact that brightness as a sensation does not obey the physical law of inverse squares, but is practically independent of the viewing distance. The explanation of this is that the size of the retinal image varies inversely as the square of the distance, just as does the amount of light reflected from the object. The two are thus in compensating relationship, and the unit density of light in the retinal image is independent of distance for a constant size of pupil. In other words, with increase of viewing distance the smaller amount of light entering the eye is concentrated into a proportionately smaller retinal image, and the projected image is therefore of approximately the same brightness whatever the viewing distance. There should be little change of brightness for different distances of viewing if the size of the pupil of the eye is maintained at these distances.

In estimating illumination the beginner may be perturbed by the fact that whereas the units and principles so far discussed use the candle as a basis of power, most lamps at present are rated

in terms of watts. This difficulty can be lessened by considering the rated luminous efficiency of lamps and the luminous efficiency of the candle. Most incandescent sources used at present for illumination are tungsten filament, gas-filled (type C) lamps. They are rated both in watts per spherical candle power and in lumens per watt. The lumens per watt rating is about 11.5 for the 75 watt size, 14 for the 100 watt size and 16.1 for the 500 watt size. Since the most commonly used lamps are the 75 to 100 watt sizes, 12.5 lumens per watt may be taken as a rough average. As has previously been noted, a standard candle emits $4\pi = 12.57$ lumens, hence in this range (75 to 100 watts) 1 watt may be taken as equal to about 1 candle power. Such approximations as we have suggested are frequently used in illumination surveys, in which precise calculations are neither worth while nor desirable. After all measurements or estimations have been made, it is usual to add as much as 50 per cent to estimated requirements because of the progressive deteriorating influence of soiled walls, ceilings and other reflecting surfaces, the gathering of dirt on bulbs and fixtures and the loss of efficiency due to aging of lamps.

The elementary concepts of lighting units and terms may be summarized thus:

1 Sources of light are rated in power terms, the unit of which is the international candle. Light sources are rated in terms of candle power or watts. For 75 to 100 watt type C lamps, 1 watt is roughly equal to 1 candle power.

2 Luminous flux is a photometric quantity, the unit of which is 1 lumen. One lumen is defined as the quantity of light required to illuminate 1 square foot to an average intensity of 1 foot candle.

3 Illumination is a photometric quantity, expressed in terms of lumens and areas.

1 lumen per square foot = 1 foot candle (ft c)

1 lumen per square meter = 1 lux (lx)

1 lumen per square centimeter = 1 phot (ph)

1 foot candle = 1,076 milliphots = 10.7 lux

4 Brightness is a photometric quantity, expressed in terms of lumens and areas. Its unit is the lambert, defined as the brightness of a perfectly diffusing surface emitting 1 lumen per square centimeter.

1 lambert = 1,000 millilamberts (mL)

An apparent foot candle, an equivalent foot candle and a foot lambert are terms for brightness describing the brightness of a perfectly diffusing surface emitting 1 lumen per square foot.

1 foot lambert

1 apparent foot candle } = 1,076 millilamberts
1 equivalent foot candle }

5 Intrinsic brilliance is a photometric quantity, expressed in terms of candle power and area. Its unit is the candle power per square inch. It is usually applied to source or transmitted light, rather than to reflected light.

PHOTOMETRY

The measurement of illumination is based fundamentally on the inverse square law of spread of illumination (fig 1). Two fields are presented to the eye for comparison, the illumination of one of which is known and that of the other is to be measured. By a comparison of the squares of the distances of the two sources, it is a simple matter of arithmetic to compute the value of the unknown illumination. Adjustment is made of the distance of one of the two sources of illumination until the two fields

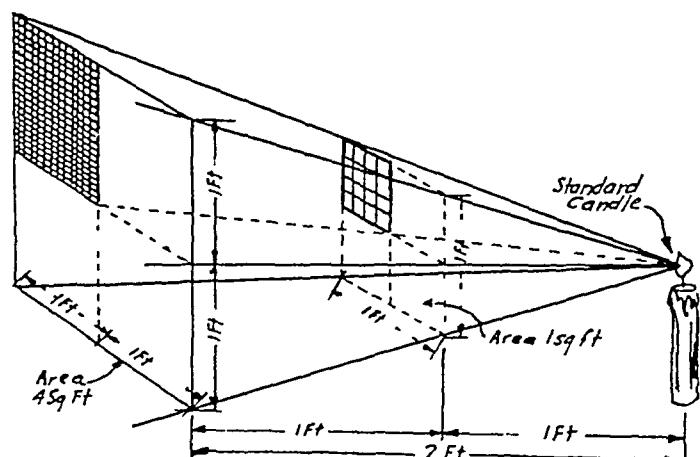


Fig 1.—Diagram illustrating the inverse square law. The amount of light received on a surface 2 feet distant from a standard candle is $\frac{1}{2^2}$ or one-fourth ($\frac{1}{4}$) the amount received at 1 foot.

are judged to be of equal brightness. Various illuminometers with calibrated scales are on the market for making these measurements readily, the best of which from a practical point of view is the Macbeth illuminometer. Still more convenient, if less accurate, are the various light meters, based on the reaction of the photoelectric cell to intensity of light. These can be used for a rough measure of the illumination at any plane, but since they are not provided with a checking device and their response to intensity of light varies with age and use, they cannot be relied on for more than a rough estimate without being frequently rechecked. Also, they are not applicable to light of a spectral composition differing from that for which they were calibrated. It cannot be denied, however, that they provide a convenient "vest pocket" means of obtaining an approximate estimate of the illumination given by tungsten lamps, for which they are customarily calibrated. Owners of a photoelectric photometer

should be cautioned that such an instrument is an extremely delicate mechanism which should be handled gently. Failure to heed this caution will soon result in an instrument which is badly out of adjustment. With gentle treatment and frequent calibration against known standards, these devices serve a useful purpose.

ILLUMINANTS

Practically all light comes from one of two sources—incandescent bodies and luminescent bodies. By far the greater portion of light used at present comes from incandescent sources. This includes sunlight, electric filament lights, arc lights and all flame sources. Such light is accompanied by a high percentage of infra-red radiation and, the amount depending on its temperature, some ultraviolet radiation. All hot bodies are inefficient sources of visible radiation.

Luminescence—light from cold bodies—is the only efficient source of visible radiation. Luminescence may be classified as follows:

1 Electroluminescence, light from cathode rays, at present is not important except for special work. This source will probably be of greater importance in the future.

2 Triboluminescence, light produced by friction and crushing, is of no practical importance.

3 Chemoluminescence is light arising from chemical action, such as the bioluminescence of fireflies and sea animals. The oxidation and reduction of the luciferin-luciferase system holds promise of future application to human needs.

4 Photoluminescence, light produced by transformation from short wave radiations into visible radiations, includes fluorescence (light produced during activation) and phosphorescence (light continuing after activation has ceased).

The most widely used form of luminescence is exemplified in the present fluorescent tube lamps, introduced in 1938. These consist essentially of a glass tube with an electrode sealed in each end. An arc is produced by current flowing between these electrodes through mercury vapor contained within the tube when the lamp is connected to the proper power supply. This arc generates some visible radiation, or light, but much more invisible ultraviolet energy, which excites fluorescent chemicals coated on the inside of the tube. Unlike the ordinary incandescent lamp, the goal of fluorescent lamps is not to produce a maximum of light directly but, rather, to generate efficiently short wave ultraviolet radiation and then to employ fluorescent chemicals or "phosphors" which can effectively convert that ultraviolet energy into visible light. A low pressure mercury arc produces an abundance of one particular wavelength

in this short wave ultraviolet region, 2,537 angstroms, and phosphors are selected and blended to respond efficiently at that wavelength. Various phosphors are used to produce different colors of light.¹

Of general artificial illuminants present use is confined almost exclusively to gas-filled (type C) tungsten filament incandescent lamps and to fluorescent lamps. The latter have various advantages and disadvantages and will be considered separately.

PRINCIPLES OF APPLICATION

The ophthalmologist is most frequently requested to give advice as to the best kind of light and the intensities required. Such questions cannot be answered categorically, since the answers will vary with the person, the task to be performed and the surroundings.

The enumeration of five general principles may here prove helpful to the ophthalmologist when he is called on to evaluate a lighting system or to give advice regarding lighting.

Intensity—A whole library might be filled with what has been written on the subject of levels of illumination, usually to the neglect of other factors, and the end has not been reached. Several catalogues of job analyses and their illumination requirements have been published by the Illuminating Engineering Society,² the American Institute of Architects and other national organizations.

In general, over the last fifty years there has been an upward trend in the recommended levels of illumination, particularly for work involving fine discrimination.

In 1896 Katz reported that 0.4 foot candle was the best average illumination when speed of reading was involved and argued that an illumination twenty-five times as intense as the threshold value was sufficient. Most authors up to 1912 recommended 2 to 4 foot candles as the optimum. In view of the lighting fixtures of those days, it is probable that the low intensities prescribed were conscious or unconscious attempts to eliminate excessive contrast or glare; moreover, light sources of high efficiency had not been developed.

Troland³ in 1931, after the most extensive review of the literature on this subject ever undertaken concluded

1 Amick, C M. Fluorescent Lighting Manual, New York, McGraw-Hill Book Company, Inc., 1942.

2 Recommended Practice of School Lighting, New York, Illuminating Engineering Society, 1938, Recommended Practice of Office Lighting, *ibid*, 1939, Recommended Practice of Industrial Lighting, *ibid*, 1942.

3 Troland, L T. Analysis of the Literature Concerning the Dependency of Visual Functions on Illumination Intensity, *Tr Illum Engin Soc* 26:107 (Feb) 1931.

the vast majority of industrial operations can be carried out at maximum efficiency with an illumination intensity in the neighborhood of 10 ft-c and many of these operations can be done equally well at 1 ft-c where contrasts and sizes of details to be perceived are not of threshold dimensions

These conclusions were strongly opposed to numerous recommendations made in the past decade, chiefly by Luckiesh and his associates at the General Electric Corporation, who argued for levels fifty to one hundred times as high as those formerly considered optimum. The argument reached the lay press,⁴ and charges were aired that the high recommendations were commercial propaganda.

The answer lies in the great range of adaptability of the human eye, which can function efficiently probably over a range of 10,000¹. It is unfortunate that so much publicity and emphasis have been given to this single factor of intensity. Ophthalmologists who are interested in getting details for a specific problem are advised to obtain a copy of the "American Recommended Practice of School Lighting" (or "American Recommended Practice of Industrial Lighting")² from the Illuminating Engineering Society. In these booklets high conservative levels are given for almost all tasks.

The effect of changes of illumination on ocular fatigue in the zones ordinarily encountered, that is, between 10 and 30 foot candles, is relatively unimportant. It is certain that continued use of the eyes, especially for fine work, under values of an order of 1 per cent of these intensities will result in eyestrain and functional inefficiency, with possible organic damage. A corresponding increase in these intensities to hundredfold values of artificial illumination will probably also result in eyestrain and ocular fatigue unless adjustment is made in the quality and distribution of the light.

Quality—The quality, or spectral composition, of light is an important attribute so far as its effect on ocular efficiency and comfort is concerned. Most authorities agree that the more nearly the quality of the light approaches diffuse daylight, the better it is. In work involving color discrimination such spectral quality is essential. Tungsten filament light is relatively deficient in green, blue and violet radiation as compared with daylight. This invalidates it for color judgments, but for all ordinary purposes it serves well. Visual acuity is good under this light, and the preponderance of yellow radiations leaves it not unpleasing or uncomfortable.

to most people. There are some persons, however, who find themselves able to work longer and with less fatigue under artificial daylight. Both of us belong in this group, and we recommend artificial daylight for others so constituted. The units manufactured by the Macbeth Daylighting Company will be found satisfactory for persons who are comfortable when working or reading under daylight but who experience discomfort when using tungsten lamps. We know of no other commercial artificial daylight product of which this can be said. The "blue bulbs," so-called daylight bulbs, do not yield light of daylight quality, or even approach it. They represent perhaps a 15 per cent step in the direction from Mazda to north skylight. For the sake of precision, we should state the quality of our illumination in terms of one of the three internationally standardized illuminants—illuminants *A*, *B* and *C* of the International Commission on Illumination. The first, illuminant *A*, may be taken as a qualitative standard of tungsten filament light in units of 200 watts or above. Illuminant *B* may be taken as the qualitative standard for white light or sunlight of apparent color temperature near 5,000 K, and illuminant *C* is the standard for "daylight" lamps, approximating light overcast skylight of a color temperature between 6,500 and 7,000 K.

Contrast—An important factor in evaluating or prescribing lighting is the contrast involved in the work being done. High contrast means increased visibility. Black on white can be discriminated very well under low illumination, whereas low contrast work requires more light. This is readily exemplified when one considers the relative visual work required to sew with black thread on black cloth and that involved in sewing with the same thread on white cloth. In the first instance a great increase in illumination is required to offset the disadvantage of low contrast. Contrast is frequently evaluated as per cent and fitted into lighting prescriptions on that basis.

For example, printing ink reflects little (approximately 4 per cent) of the light incident on it. Good white paper reflects about 80 per cent of the light incident on it. The contrast of such ink and paper, then, is 4 per cent on 80 per cent, or 76/80, which equals 95 per cent. If the ink reflects 8 per cent, the percentage contrast is 8 per cent on 80 per cent, or 72/80, which equals 90 per cent. In evaluating the illumination to be used in reading, the following illustration may be used. The material is printed in 8 point type, with an average blackness of

8 per cent (reflectance). The paper has an 80 per cent reflectance. The brightness contrast is therefore 90 per cent. For such reading an illumination of 10 to 15 foot candles is recommended. This level should be increased if (1) the visual angle is smaller, as with 6 or 4 point type, (2) the contrast is less, as when the paper is old, yellowed, smudged or of poor quality, (3) speed and accuracy are needed, as in proof-reading, (4) the subject has poor eyes or a refractive error, (5) the subject has poor visual acuity with the best possible correction, or (6) the work requires prolonged periods of concentration. Good lighting in such a case increases visual efficiency, speed of seeing and comfort.

Distribution.—Distribution is an important factor in good lighting. Glare and its evil consequences, although a result of faulty distribution, will be considered separately. The distribution of light in the field of vision affects all the component visual functions, as well as the integrated act itself. However optimal other conditions may be, extreme variations in intensity occurring in the field of vision produce disturbing effects on the eye, and the disturbance is directly proportional to the size and intensity of the disturbing source and its proximity to the line of sight. Under certain conditions these extreme contrasts are desirable, as when an object near the threshold of acuity must be made visible, but in general pronounced and useless differences in brightness in the field of vision contribute to ocular inefficiency and the production of fatigue. This is especially true when the eye in its movements must subject the central portion of the retina to frequent and sudden changes in intensity of stimulus, the inability of the macula to meet these demands for repeated rapid adjustment results in temporary partial blindness—central scotoma. For greatest comfort the entire field of vision should be well and evenly illuminated, with perhaps a mild increase in the area of the working plane.

Unsteadiness of illumination is another source of fatigue, by producing incessant demands on the eye for readjustment. Under certain conditions, such as flicker, it is quickly and unpleasantly effective. Cloud or smoke shadows frequently cause rapid and annoying alterations in light values near windows.

Diffusion is related to distribution and shares its importance. Diffuse light does not cast sharp, dense shadows. As with contrast, under certain conditions these sharp shadows may add to visual efficiency, but these special conditions do not detract from the general statement that the more diffuse the light the better it is tolerated by

the eye. Lancaster has characterized diffusion as an important quality of good lighting and has indicated a rough test for this quality. A pencil held a few inches from the paper, book or work to be viewed should not, and will not, cast a sharp shadow if the light is properly diffused.

Glare.—Glare is a factor in faulty distribution. Glare has been defined as useless light in the field of vision. Its importance increases as it approaches a position on the line of sight. Glare may be diffuse, specular or direct. Diffuse glare is the type experienced outdoors from too high intensities. Specular glare is the type produced by mirrors, highly polished metal and furniture, glossy paper and other shiny surfaces. Light specularly reflected from an object is not focused into an image on the retina. It is represented merely by a spot of unfocused light. If focused, it would form an image of the source of light, not of the reflecting object. However, in looking at an object one focuses for it, not for the source of light. Light diffusely reflected, since it begins its effective origin at the reflecting surface, forms an image alone of that surface on the retina. One thus sees objects only by diffusely reflected light. The light specularly reflected, since it forms an overlay of unfocused light on the image, blurs that image and is therefore not an aid, but a hindrance, to vision. There are three methods by which one may combat this type of glare. (1) The direction of the light may be changed, (2) the light may be completely diffused, or (3) specular reflection may be eliminated, partially at least, by Polaroid. Of the three methods, the first is the most practical and least expensive. Rhoads⁵ gave a test for this type of glare. A fairly large mirror is placed on the working plane or where a book is to be held for reading. If any light sources can be seen in the mirror, then the working plane, the position of the body or the light source should be adjusted until the reflections disappear. Another method by which one may ameliorate, though not wholly avoid, such specular reflection is to make the light sources as extensive as feasible, thereby permitting a reduction in their intrinsic brilliance without reducing the illumination.

Direct glare arises from bright objects in the field of vision, such as headlights out of doors or unshaded lamps indoors. The unpleasant effects of such sources of glare are, as already stated, directly proportional to the brilliance of

5. Rhoads, J. N. A Reflecting Book Marker for Teaching Readers How to Avoid Eye Strain, Ophth Rec 2 416-419 (Aug) 1913

the object and its proximity to the line of sight, so that a 100 watt lamp 10 degrees from the line of sight will produce about as much glare as a 200 watt lamp 15 degrees from the line of sight. In order to avoid or reduce glare, the brilliance of light sources should be kept as low as possible. Reduction in the brilliance of the source will reduce the illumination unless compensation is made, and this compensation takes the form of increase in the area of the source. Hence large sources of low intrinsic brilliance, achieved through luminaire design, diffusing glasses or semi-indirect lighting, are distinctly preferable to small, bright sources (fig. 2). The whole evolution of lighting engineering in the past two decades has been in this direction. An excellent rule for one to follow in evaluating or prescribing such compensation is that the brightness of the

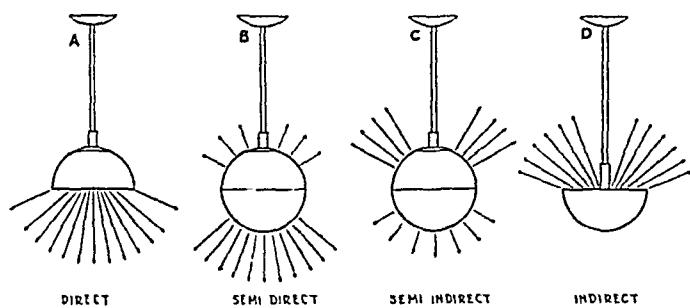


Fig. 2—Types of lighting fixtures

In this figure *A* shows direct lighting *B*, semidirect lighting, *C* semi-direct lighting and *D*, indirect lighting.

Three decades ago most lights had either no fixtures or were equipped with fixtures of type *A*. At present luminaires are preponderantly of type *C*.

source shall not be more than twenty (preferably ten) times the brightness of its background and, further, that the intrinsic brightness of the source shall not exceed 3 (preferably 1) candles per square inch.

A few rules of thumb suggestions may be helpful to one in evaluating or prescribing for an illumination situation.

1 The intensity of light, or the illumination level, is to be selected with reference to the patient and the nature of the work he is to do.

2 The quality is evaluated with reference to the task to be performed and the patient's preferences. Illuminant *C*, standardized by the International Commission on Illumination, is mandatory for most work involving color judgments and is preferred for general purposes by a large number of subjects.

3 The conditions of contrast have an important bearing on the intensity and quality recommended.

4 The distribution should be as even and diffuse as possible. Pronounced differences in brightness should be avoided. The Lancaster test for diffusion is helpful.

5 Glare is to be looked for and ameliorated or avoided. The Rhoads test for specular glare is helpful.

The background is to be kept diffusely illuminated. A good rule is that the ratio of illumination of the working plane to the background shall not exceed 4:1, and preferably should be less. The ratio of brightness of the source to that of the background should not exceed 20:1, preferably 10:1, and the intrinsic brilliance of the source should not exceed 3 (preferably 1) candles per square inch. In order to achieve an evenly diffuse illumination of 15 to 20 foot candles in a room with light walls and ceilings, there will be required (if a tungsten filament type *C* illuminant is used) about 2 to 3 watts per square foot of floor space. Higher general levels are rarely required and should not be recommended except under special circumstances, since the excessive infra-red radiations of such sources (90 per cent) would cause unpleasant heating in the summer time and might necessitate air conditioning.

FLUORESCENT LIGHTING

The ophthalmologist will frequently be requested to give advice concerning the fluorescent tube lighting, introduced in 1938. This type of lighting has been growing in use and importance. In spite of six years of development, much is to be desired, and it is too early to give an unqualified opinion. It is obvious that one great fault has been inadequate design of fixtures to hold these tubes. The present period may be analogous to the middle teens, after the introduction of the gas-filled, unfrosted Mazda lamp. The present fluorescent tubes are too bright for comfort when unshielded, and most installations carry little or no shield. The intrinsic brightness of the 30 watt Mazda F lamp is 5.5 candles per square inch for the 3,500 degree white light tube and 4.5 candles per square inch for the daylight tube. All Mazda fluorescent tubes, except for the 14 and 15 watt types, have a brightness of over 3 candles per square inch.

When the lamp is used close to the work, as a desk lamp in the usual position at the back of the desk, the glare from specular reflection is pronounced. This fault is partially obviated if the lamp is placed along the side of the desk or table, on the left side for a right-handed person and on the right side for a left-handed person.

The advantages of the fluorescent tubes are their high lumen per watt efficiency and the flexibility, within a limited range, with which their color value can be changed.

They do not, however, and probably cannot be made to, give the spectral curve of daylight, and time and experience are necessary to show whether deviations in this respect are deleterious. The fluorescent tubes are best suited for installations in large areas and are particularly useful in air-conditioned interiors because of their relatively low heat output. They should always be mounted high. Their recommendation for small rooms in the present state of development of the lamps and fixtures is questionable.

Many people, sensitive and insensitive, work happily, efficiently and comfortably under fluorescent lighting. Many others, and they are not neurotic or reactionary persons incapable of absorbing new ideas, have experienced discomfort and great unpleasantness since the installation of fluorescent lighting. Common complaints are ocular fatigue, burning of the eyes, headache, tearing and a feeling of sand in the eyes.

At the Knapp Memorial Laboratories, where studies on fluorescent lighting have been carried out, we have been inclined to explain the unpleasant effects of this type of lighting in terms of six factors: (1) flicker, either (a) total or (b) electrode, (2) spectral quality, (3) high intrinsic brightness, (4) radiation of wavelength of 312 to 313 millimicrons, (5) lag of emission in the blue-green-yellow portion of the spectrum, and (6) stroboscopic effect.

The total flicker is usually due to insufficient voltage or to deteriorated lamps, although electrode flicker has frequently been seen when neither of these factors was apparently present. The spectral quality, we are sure, affects color vision and may produce unpleasant psychologic effects. Probably the chief difficulty arises from the high intrinsic brightness, which varies from 5.5 candles per square inch, in the 30 watt white

light tube, to 3.3 candles per square inch, in the 40 watt daylight tube. We strongly believe that intrinsic brightness should be kept below 3, preferably 2, or even 1, candles per square inch. We feel sure that diffusing covers for fluorescent tubes will be used more and more in the future.

Fluorescent tubes emit a fairly strong double line at 312 to 313 millimicrons. Some of this radiation may pass through the glass of the tube. Quantitative measurements are at present under way to evaluate this factor, which may prove to be important. Ultraviolet radiation of this wavelength might have two effects. Such rays are abiotically active, and since the effect of such radiation is cumulative, prolonged exposure might result in irritation of the cornea and conjunctiva. Another, and so far unconsidered, effect is the intraocular fluorescence which might be produced if this radiation reaches the lens of the eye, in this case the overwash of fluorescent light generated within the eye might be very unpleasant.

The lag of emission of the blue-green-yellow components from a fluorescent tube results from the difference in excitation periods of the various phosphors used in coating the tube and may easily be demonstrated by observing such a tube in action through a stroboscope. There is a large, brief, blue peak, followed by other component colors. Whether this "blue beat," or the lag of emission of the other colors, has any visual, physiologic or psychologic significance is not yet known.

Finally, the well known stroboscopic effect of fluorescent lights makes them unpleasant for the illumination of rapidly moving machine parts. This effect can be partly overcome by use of multiple, out of phase tubes, but the best ratio so far achieved has been 3 to 1 (a Mazda incandescent lamp being used as 1). Fluorescent lighting should not yet completely displace the more conventional types.

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ANALYSIS OF CASES OF ANISEIKONIA

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The doubts enumerated in an editorial by Crisp¹ suggested the following presentation of and comments on cases of aniseikonia.

The patients who come for examination for aniseikonia have been well described by Post²

[They are] only those whom he [the ophthalmologist] has failed to relieve with the usual lenses and who, in general, are bothered by ocular as well as other trivialities and often have exhausted his patience. Thus, the aniseikonic clinics have become the rendezvous of the most difficult patients for whom to obtain comfort. That *anything* good is accomplished for these patients is the miracle.

Crisp's first question was how large a proportion of the ocular difficulties apparently relieved by prescription for aniseikonia were capable of relief in no other way, and, second, what proportion could have been relieved by more complete accuracy in refractive measurements without the aid of size lenses.

(table 1), and of this number 97 examinations were complete enough to allow for analysis. Sixty-one patients showed an appreciable amount of aniseikonia, 17 showed no aniseikonia, and 19 had such poor fusion that examination was

TABLE 1—Data on Patients with Aniseikonia

Patients with aniseikonia	
Comfort with isekonic lenses	14
Improvement with isekonic lenses	3
No improvement with isekonic lenses	4
Reading difficulties	3
Patients reexamined	20
Patients with no aniseikonia	17
Patients with poor fusion	19

impossible until after some form of muscle training.

Isekonic lenses were ordered for 24 patients, and of this number 14 stated that they had obtained complete comfort, with disappearance of

TABLE 2—Data on Three Patients with Reading Difficulties Given Isekonic Lenses

Name	Age, Yr	Improve ment	Prescription	Comment
B	17	+	(R) +2.50 D sph ⊖ -0.50 D cyl, ax 165, vision 20/16 (L) +2.50 D sph ⊖ -0.50 D cyl, ax 15 ⊖ 0.50% over all magnification ⊖ 1.50% meri- dional magnification, ax 90 (vision 20/16) September 1942	Divergence insufficiency, reading ability improved, no symptoms of asthenopia
N	10	+	(R) -0.75 D sph ⊖ 0.75% over all magnifi- cation (vision 20/20) (L) -0.50 D sph (vision 20/20) November 1943	Considerable improvement the first two months. Patient did better later, but performance not up to average or to his intelligence quotient
M	16	+	(R) +2.75 D sph ⊖ -0.75 D cyl, ax 25 ⊖ 1.5 Δ (vision 20/13.2) (L) +2.50 D sph ⊖ -0.75 D cyl, ax 150 ⊖ 1% meridional magnification, ax 180 (vision 20/15) September 1941	Convergence insufficiency alternate macular sup- pression September 1943. Aniseikonia un- changed, reading ability improved, with correc- tion of muscle balance

Since September 1942 I have made the examinations for aniseikonia of the patients referred to the department of ophthalmology of the Northwestern University Medical School. One hundred and seventeen examinations have been made.

From the Department of Ophthalmology, Northwestern University Medical School

Read at the Eightieth Annual Meeting of the American Ophthalmological Society, May 29, 1944, Hot Springs, Va.

1 Crisp, W. H. Aniseikonia Doubts, editorial, Am J Ophth 26:1329 (Dec) 1943.

2 Post, L. T. Future of Aniseikonia, editorial, Am J Ophth 26:321 (March) 1943.

their asthenopic symptoms. Three reported that the condition was improved, and 4 noticed no improvement.

Of this number, 3 students, aged from 10 to 17, who had reading difficulties were given isekonic lenses after a complete general study and remedial reading efforts had given little help (table 2). The 3 patients showed some improvement immediately after use of the lenses. The high school student in his last year, as a senior, did the best work of his twelve years in school but continued to find reading a slow process. The other high school student, in her first year, im-

lar suppression or convergence insufficiency. Two of these 7 patients were able to take off their glasses except for reading when the muscle balance was improved. Two had associated glandular dyscrasia, and the glasses were discarded after specific medication. The measurements of the size difference of the images was found to be practically the same for all patients as the values obtained at the previous examinations.

The 19 patients for whom the examination was entirely unsatisfactory had poor binocular vision, which included poor fusion with suppression, poor amplitude, divergence insufficiency or convergence insufficiency. These patients were instructed to return for reexaminations after improvement of the muscle balance.

Careful refractive corrections first is answered by the results with the patients who were made comfortable with theiseikonic lenses, since the majority of these patients had worn the same prescription for their refractive correction before size magnification was added, it is to be pointed out, also, that their muscle balance was normal or was restored to normal with simple treatment.

In answer to the second question, as to what proportion of ocular disturbances could have been relieved by greater accuracy in refractive measurements without the aid of size lenses, the corrected vision of the patients was excellent as a rule, and the refractive measurements were usually accepted, but the ocular muscle balance was frequently inadequate, and a satisfactory examination for aniseikonia was not possible until

TABLE 7.—Data on Patients Who Were Uncomfortable with Iseikonic Lenses

Name	Age, Yr	Occupation	Muscle Balance	Prescription	Comment
E	52	Salesman	Left hyperphoria 1	(R) -0.50 D sph \odot -0.50 D cyl, ax 145 \odot 1 Δ base up (vision 20/16) (L) -1.25 D sph \odot -0.50 D cyl, ax 180 \odot 1.5% meridional magnification ax 180 (vision 20/16) April 1942	Eyes comfortable for short period after adjustment of eye wire distance same glasses previously without magnification
F	44	Housewife	Convergence insufficiency	(R) +1.00 D sph \odot -0.25 D cyl, ax 30 \odot 0.75% over all magnification (vision 20/20) (L) +1.25 D sph \odot -0.50 D cyl ax 150 (vision 20/16) +1.50 D sph added February 1943	Glasses for distance comfortable, reading glasses no help
G	61	Housewife	Normal	(R) +2.00 D sph \odot -0.50 D cyl, ax 180 \odot 2% meridional magnification, ax 90 (vision 20/16) (L) +2.25 D sph \odot -0.50 D cyl, ax 175 \odot (for reading) +1.75% magnification June 1943	Glasses good only for objects at arm's length discarded after two weeks
M	47	Office work	Normal	(R) +3.00 D sph \odot 4% meridional magnifica- tion ax 90 (L) +2.00 D sph (Jaeger test type 4) June 1943	Reading glasses only

Some of the remaining 17 patients who had aniseikonia of varying amounts had symptoms which indicated a general disturbance, and they were advised to return after this condition had received attention. Two patients would not order the glasses for cosmetic reasons, and some patients are receiving muscle training.

Any patient with an oblique astigmatism and a size difference should be tested with the space eikonometer, as this adaptation is not available for the standard eikonometer, this may account for failure in some cases.

COMMENT

The answer to Crisp's question of how large a proportion of the ocular difficulties apparently relieved by prescriptions for aniseikonia could have been relieved if the patients had worn the

binocular fusion was improved and until it could be maintained. With improvement in the maintenance of binocular fusion, several of the patients were as comfortable without the glasses as with them.

It was also notable that many of the patients had never had any particular ocular discomfort until vision was improved with glasses, especially at the age of presbyopia, when it became necessary for them to wear glasses. Then improved vision, with the binocular attempts, brought out asthenopic symptoms.

In conclusion, binocular fusion and ocular muscle balance, together with refraction and size magnification should be considered of basic importance, for the comfortable use of the eyes as the "seeing organ."

UNUSUAL FORMS OF NYSTAGMUS

WITH A REVIEW OF THE LITERATURE

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The purpose of this article is to discuss several unusual and comparatively rare forms of nystagmus which we have seen and to present a detailed report of a case. Two types of ocular nystagmus voluntary and occupational, and a form of mixed nystagmus due to compression of the upper cervical portion of the cord, are considered.

Fundamentally nystagmus may be of vestibular, cerebellar, cerebral, upper cervical or ocular origin. The optic system is involved in all forms, but it is only in the ocular type that it is directly affected. In all other cases it is involved indirectly by way of the vestibular system. The vestibular system may be the seat of origin of irritative phenomena and transmit the abnormal impulses to the ocular system, or the pathologic change may be in the cerebrum, the cerebellum or the upper cervical portion of the cord, in which event the vestibular system together with the posterior longitudinal fasciculus, acts as a nucleus for the mediation of the abnormal impulses.

REPORT OF CASES

CASE 1—*Mixed nystagmus, secondary to compression of the upper cervical portion of the cord*

A young soldier was admitted to the orthopedic section of the Walter Reed General Hospital, Washington, D. C., in the fall of 1941, with a compressed fracture of the body of the third cervical vertebra and mild involvement of the spinal cord. Reduction was successfully carried out, and halter traction was applied. The patient remained well for about four weeks, then occipital headache developed, and he complained of constant motion of objects with fixation of the eyes and slight numbness of the upper extremities. Neurologic examination revealed nothing significant except for a slight degree of hypesthesia, incomplete, in both arms and notable bilateral rotary nystagmus on direct gaze, in accommodation both for the near and for the far point. On lateral gaze, the rotary nystagmus disappeared and was replaced by bilateral horizontal nystagmus, the quick component being in the direction of gaze. The signs were interpreted as due to compression of the spinocerebellar pathways. Roentgenograms showed fairly good reduction of the fracture, although there was slight displacement. Further manipulation and traction were performed, and the symptoms finally disappeared. The patient had an uneventful convalescence.

CASE 2—*Volitional nystagmus*

A young private was admitted to a general Army hospital in the winter of 1943, complaining of weakness and stiffness of the muscles of the legs and arms. When, in the course of routine neurologic examination, the patient was requested to follow a cotton applicator with his eyes, he promptly volunteered that he could at will move his eyes back and forth at a very fast rate, and he seemed proud of the fact. When he was asked to demonstrate this phenomenon, he promptly produced a bilateral horizontal nystagmus, of pendular type, fast rate and large amplitude. He stated that he could keep up the motion for an indefinite period were it not that after fifteen or twenty seconds he became light headed and his eyes became tired. Another case of volitional nystagmus has been seen by one of us (H. C. S.).

CASE 3—*Occupational nystagmus*

A sergeant aged 28, white, a draftsman, was admitted to an Army station hospital on Sept. 1, 1943, with the complaint of blurring of vision and a sensation of jumping of objects in the horizontal plane. He was transferred to an Army general hospital on September 10, with the diagnosis of severe bilateral horizontal nystagmus, of undetermined cause. Vision was 20/50 in the right eye and 20/50 in the left eye.

History.—The patient was inducted into the Army on July 12, 1940. Vision at that time was 20/30 in each eye, and he had no complaints referable to the eyes. The past and family histories were without significance. Two months after induction the patient commenced work as a map plotter, doing a considerable amount of close work which involved plotting and triangulation.

Present Illness.—The first symptoms appeared in March 1941, approximately six months after the map work was begun. After about five hours of work he experienced a sensation of drawing and aching in the region of the supraorbital ridges, accompanied by slight blurring of vision and the sensation of jumping of objects in the horizontal plane. The duration of these attacks was ten to fifteen minutes. A brief rest was followed by relief, and work could be resumed. During the course of the next few months the attacks became more frequent, and a longer period of rest was required before the symptoms disappeared. Finally, however, the periods of rest gave only partial relief, and by June 1941 the patient was forced to do only part time work. Vision at that time was 20/50 in each eye.

During the course of the next two years the patient continued to work with maps as a part time job, and he noted that prolonged use of the eyes greatly aggravated the blurring of vision and the sensation of jumpiness of objects. Rest afforded some relief, although more or less permanent blurring and the sensation of to and fro motion of objects persisted. Vision in February 1943 was 20/100. At that time, however, he was doing class work at school in addition to the map work and was using his eyes constantly.

He continued to work until the time of his admission to the hospital. No progression or remission of symptoms had been observed in the six months prior to his admission.

Examination—Physical examination, including a complete ophthalmologic and neurologic study, revealed nothing abnormal except for the ocular condition. Vision was 20/50 in the right eye, with ability to read Jaeger test type 1, and 20/50 — 1 in the left eye, with ability to read Jaeger test type 2, and was uncorrectable. The fields of vision were normal.

External examination revealed a moderate degree of horizontal nystagmus. The pupillary reactions were normal, and the pupils were round and equal on the two sides. The transparent media were normal. Slight blurring of the nasal sides of the optic disks was present, but this appeared to be within normal limits. The tentative diagnosis was nystagmus of ocular type, not associated with a neurologic condition. This opinion was confirmed by repeated careful neurologic examinations. The oscillation of the eyeballs was in the horizontal direction, and the components of the nystagmus were of equal rate and amplitude, so that a pendular type of motion resulted. Lateral gaze produced slight exaggeration of the rate but did not affect the amplitude. The nystagmus was not influenced by accommodation. There was no indication that the condition was of vestibular (labyrinthine), cerebellar or cerebral origin.

The diagnosis was severe bilateral horizontal nystagmus of ocular type and occupational origin.

COMMENT

The occurrence of nystagmus with lesions of the cord is uncommon. A review of the literature, however, indicates that a number of cases have been reported. It is assumed that in case 1 the nystagmus was the result of interference with the spinocerebellar pathways, resulting in abnormal stimulation of the cerebellum, which, in turn, involved the optic system. Oppenheim¹ stated that nystagmus may occur in cases of involvement of the spinal cord.

About 12 cases of voluntary nystagmus have been reported in the literature. The nystagmus was of the horizontal type. Rea² stated that voluntary nystagmus has been described by Pyle and Ball and others. Cases of both the unilateral and the bilateral form have been reported. Persons with voluntary nystagmus have never had true nystagmus. According to Bing,³ nystagmus not infrequently occurs in cases of hysteria, and nystagmus may be produced voluntarily by the hysterical person. Hysterical nystagmus, unlike the oscillating nystagmus caused by an organic lesion, is jerky and irregular.

¹ Oppenheim, H. Textbook of Nervous Diseases, translated by A. Bruce, Edinburgh, O. Schulze & Co., 1911, vol 2, p 703.

² Rea, R. L. Neuro-Ophthalmology, ed 2, St Louis, C. V. Mosby Company, 1941, vol 3, pp 65-71.

³ Bing, R. Textbook of Nervous Diseases, St Louis, C. V. Mosby Company, 1939, chap 30, p 779, chap 2, p 93.

With 3 exceptions, miners' nystagmus excluded, a review of the literature of the past twenty-five years failed to reveal any case of occupational nystagmus. Fuchs⁴ referred to the occurrence of nystagmus in composers, which he ascribed to a strained position of the eyes. Wilson⁵ reported cases of nystagmus occurring in train dispatchers and crane workers. McCord⁶ gave an excellent description of occupational nystagmus in train dispatchers. He reported 81 cases, in all of which the nystagmus was of the horizontal type. The condition is accepted to be of occupational origin and is attributed to continual motion of the large train sheet beneath the eyes and the movement of the head and eyes over the train sheet, both necessary in the continual recording of data concerned with movements of trains. McCord also stated that among jewelers, draftsmen, composers and persons doing similar close work nystagmus had occasionally been encountered. (In 1 instance a train dispatcher who had not followed his occupation for eight years was observed still to exhibit nystagmus.) McCord⁶ also stated that while it requires fifteen to twenty years for miners' nystagmus to develop, the other forms of occupational nystagmus may appear after as little as one year of work at the particular trade. These forms of occupational nystagmus are not as severe or incapacitating as is miners' nystagmus.

The pathophysiology and the pathogenesis of occupational nystagmus are the result of the interaction of several factors, namely, poor and improper illumination, the mechanical to and fro movement of the eyes incident to the particular occupation, and retinal fatigue. Adequate illumination is important in that the strain is relieved and the factor of retinal fatigue is minimized. This is the all-important factor in miners' nystagmus, so much so that the condition is practically nonexistent when miners are provided with proper illumination. The mechanical factor (the to and fro movements) may be interpreted as a coordinated and purposeful act primarily provoked by an external stimulus which is of the nature of an occupation requiring synchronized ocular activity. Constant repetition leads to habitual and involuntary reproduction.

⁴ Fuchs, E. Text-Book of Ophthalmology, ed 8, edited by A. Duane, Philadelphia, J. B. Lippincott Company, 1924, p 342.

⁵ Wilson, S. A. K. Neurology, edited by A. N. Bruce, Baltimore, William Wood & Company, 1940, vol 2.

⁶ McCord, C. P. Occupational Nystagmus, in Train Dispatchers, J. A. M. A. 96:1131 (April 4) 1931.

of the act, which for no other purpose assumes the nature of an irrepressible impulse. Both inopportune and excessive, the act develops into a habit spasm, or tic, so that what started to be a physiologic adaptive process actually resolves into a pathologic condition. The added factor of retinal fatigue facilitates the establishment of the habit, so that a dilemma is presented. In this respect nystagmus may be looked on as a compensatory mechanism incited by an attempt at avoidance of retinal fatigue by engaging more retinal elements in the visual effort and protecting other retinal elements. Casten⁷ stated the belief that nystagmus possibly results from the attempt at stimulation of more retinal elements in order to improve vision and stressed the importance of change of occupation, which he felt to be imperative. Mackie⁸ stated that nystagmus is unknown in India, where the miners alternate mining with agriculture. He expressed the opinion that nystagmus is a physiologic adaptation, but with potential risks in the event of loss of control. Krieg⁹ pointed out that the

7 Casten, V. G., in Berens, C. *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936, chap 52, p 968.

8 Mackie, E. S. *Miners' Nystagmus*, Brit M J 2 258 (Aug 1) 1936.

9 Krieg, W. J. S. *Functional Neuroanatomy*, Philadelphia, The Blakiston Company, 1942, chap 9, p 130.

disturbance of the optic system which produces nystagmus may be due to lack of development of the macula, very poor vision, dim light or visual fatigue. All these conditions dispose to inability to fix the macula on a point. The two components of ocular nystagmus are usually of uniform rate, i.e., the slow and the rapid component lack differentiation. Rea,² in discussing macular function, stated that nystagmus was a physiologic adaptation in an effort at the prevention of fatigue. Citing Healy, he stated "At first the oscillations are a physiological psycho-optical reflex, they become eventually a pathological habit-spasm." Bing³ suggested that since optic nystagmus occurs in persons who are amblyopic, the afferent arc through which the altered impulses are propagated may be the proprioceptive fibers, originating in the extraocular muscles, and not the optic nerve. With defective conditions of the retina, the nystagmus is brought about by the patient's straining the muscles in order to obtain a better definition of the object. Such conditions include albinism, loss of macular rods occurring in persons, such as miners, who work in dim light, and various other conditions producing blindness. This type of nystagmus may be an ocular device to "spread" the image over more rods and cones and thus to obtain better vision.

DIBUTOLINE SULFATE

A NEW MYDRIATIC AND CYCLOPLEGIC DRUG

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There has been need in ophthalmology for new mydriatic and cycloplegic drugs. Hypersensitivity and idiosyncrasies to atropine and its derivatives are not uncommon. Also, the dosage of the more potent members of the group is limited by undesirable systemic effects, e.g., excitation and depression of the central nervous system, flushed face and drying of secretions. Finally, the ocular effects of atropine and scopolamine are unduly prolonged and are not readily counteracted. Recently we have synthesized the first substitutes for the atropine series effective on the eye.¹ The new mydriatic and cycloplegic drugs are surface active carbamic acid esters of the choline type and, therefore, are chemically unrelated to atropine. The ocular effects of the first of the new class of drugs have been reported previously.² Herein are described the ocular pharmacologic effects and some clinical applications of dibutoline, a name for the latest and most effective member of the series.

Dibutoline sulfate (dibutylcarbamate of dimethylethyl-β-hydroxyethyl ammonium sulfate) is chemically related (fig 1) to carbaminoylcholine chloride but has different physical properties and antagonistic pharmacologic effects on the intraocular muscles, i.e., dibutoline is surface active and mydriatic, while carbaminoylcholine is surface inactive and miotic. Sulfate salts of dibutoline occur as white crystals which readily dissolve in water to form a clear, colorless solution with a slightly bitter taste and

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1 Swan, K C, and White, N G Some New Choline Esters with Cycloplegic and Mydriatic Action, Proc Soc Exper Biol & Med 53:164-166 (July) 1943

2 Swan, K C, and White, N G (a) Choline Esters with Atropine-Like Action, J Pharmacol & Exper Therap 80:285-288 (March) 1944, (b) Di-N-Butyl-Carbaminoylcholine Sulfate A New Mydriatic and Cycloplegic Drug, Arch Ophth 31:289-291 (April) 1944

a faintly aromatic odor. Heat and light result in slow decomposition, but the solutions are stable at room temperature for weeks. Partially decomposed solutions become less potent, but the decomposition products are not toxic. The new drug is not an alkaloid and therefore does not have the considerable chemical incompatibilities of atropine.

Dibutoline sulfate should be dissolved in distilled water. In a saline or buffer solution dibutoline forms salts, e.g., dibutoline chloride, which are considerably more surface active than the sulfate and therefore more likely to cause

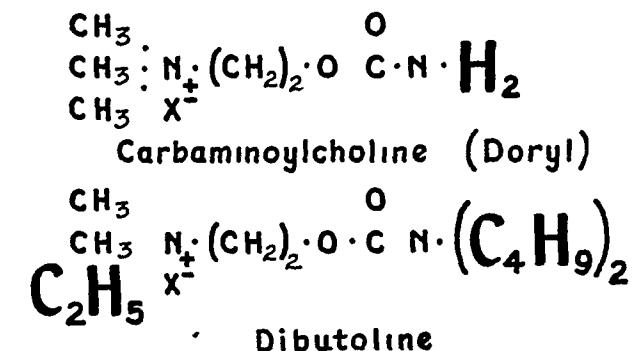


Fig 1.—Formula for carbaminoylcholine chloride and dibutoline sulfate

conjunctival irritation. A solution of 5 per cent dibutoline sulfate in distilled water is nearly neutral (p_{H} 6.5), is of almost the same osmotic pressure as isotonic solution of sodium chloride and has an air-water interfacial tension of 47 to 48 dynes per cubic centimeter at 25°C.

Dibutoline produces paresis of smooth muscles innervated by the parasympathetic nervous system. Its effects on the smooth muscles of the eye, therefore, simulate those of paralysis of the oculomotor nerve, i.e., dibutoline produces paresis of the sphincter of the iris and the ciliary muscles. The action of dibutoline on the intraocular muscles is antagonistic to that of pilocarpine, physostigmine, acetylcholine and carbaminoylcholine.

Dibutoline has no effect on the ocular muscles innervated by the sympathetic nervous system, i.e., the smooth muscle of the lid and the dilator

fibers of the iris. It does not produce widening of the palpebral fissure, which is effected by epinephrine, cocaine and related compounds, neither does it significantly alter reactivity of the dilator fibers of the iris to electrical stimulation of the cervical sympathetic nerve or to stimulatory drugs. Mydriasis produced by the new drug, therefore, may be enhanced by administration of epinephrine or related compounds, which act by stimulating the dilator fibers.

The relative potency of dibutoline sulfate and of homatropine hydrobromide was studied on the iris of the albino rabbit. Intravenous in-

Although when they were given by intravenous injection homatropine and dibutoline were of equal potency, when the two drugs were given by instillation dibutoline was more effective on the rabbit eye. This difference in potency seemed largely due to the more effective corneal penetration of dibutoline, for only slightly less dibutoline than homatropine was required to produce a comparable degree of mydriasis when the two drugs were injected into the posterior corneal layers or into the anterior chamber.

In the human eye, 5 per cent solutions of dibutoline sulfate and of homatropine hydro-

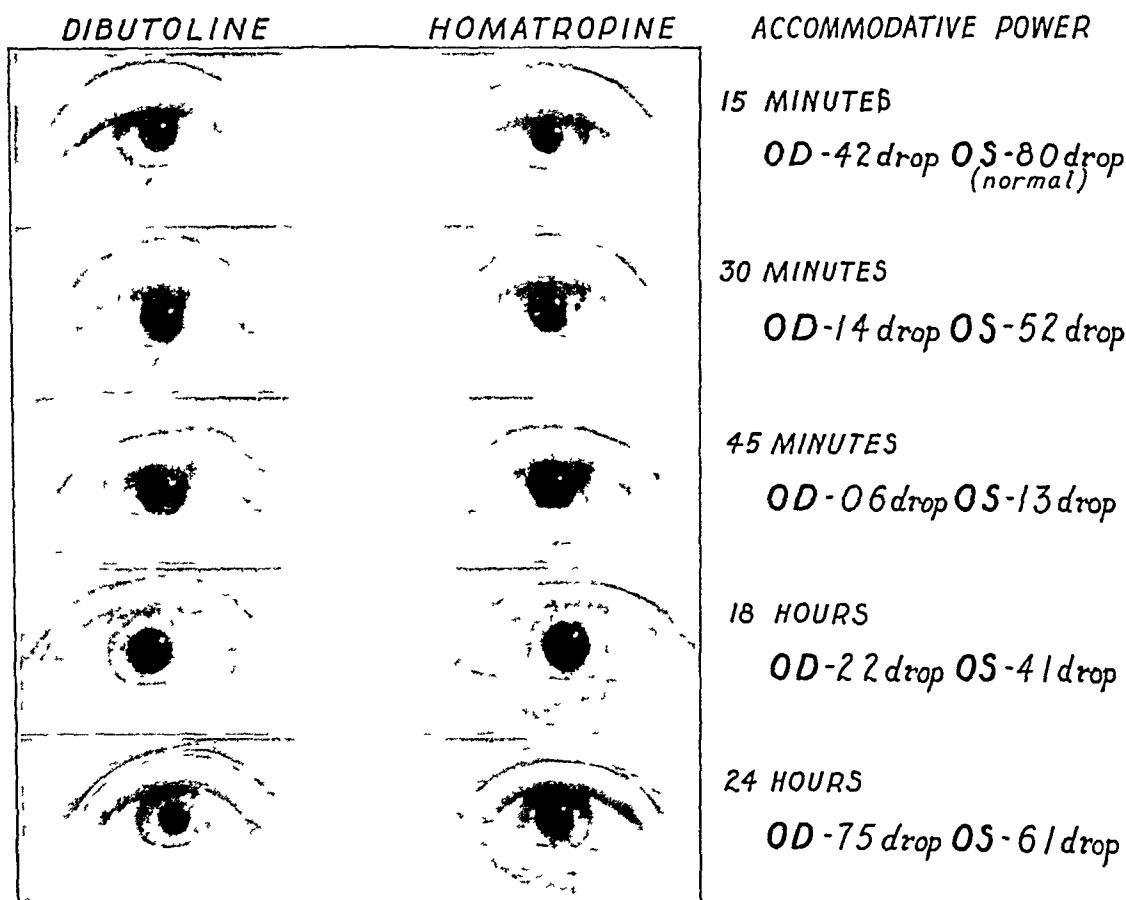


Fig 2.—Onset and duration of mydriasis and cycloplegia in an emmetropic adult following single instillations (0.075 cc.) of a 5 per cent solution of dibutoline sulfate in the right eye and of a 5 per cent solution of homatropine hydrobromide in the left eye.

jections of 1 per cent solutions of the drugs were made in 10 animals to determine the minimal dose of each drug producing dilation of the pupil and loss of the light reflex. Two to 5 mg per kilogram of body weight of each of the two drugs injected intravenously usually produced an immediate increase of 4 to 5 mm in the horizontal diameter of the pupil, while injection of 10 mg per kilogram of body weight resulted in total loss of the pupillary reaction to light. No synergism between the two drugs was demonstrated, i.e., 5 mg of each of the two drugs injected simultaneously had approximately the same effect as 10 mg of either drug injected separately.

bromide usually produce equivalent degrees of mydriasis, but the minimal dose of homatropine producing mydriasis is less than that of dibutoline. The latter, however, is the more effective cycloplegic. Moreover, mydriasis and cycloplegia produced by the new drug develop and wear off simultaneously, consequently, the size of the pupil and its reactivity provide convenient and reliable indications of the degree of cycloplegia produced by dibutoline. In contrast, the effects on the iris of the atropine series of drugs are much more intense than the effects on the ciliary muscles. In some young adults it is possible to induce almost complete mydriasis with neg-

ligible loss of accommodation by means of frequent small doses of homatropine

Twenty-four young adults had refractions under cycloplegia induced both with dibutoline and with homatropine to determine the relative effectiveness of the two drugs as cycloplegics. At the first examination the right eye received a 5 per cent solution of dibutoline sulfate and the left eye an equivalent dose of homatropine hydrobromide. A week later the process was reversed. Minimal residual accommodation was determined by adding a +3.00 D sphere to the cycloplegic correction for distance and determining the nearest point at which the patient could read standard 0.5 print in constant artificial illumination. Minimal residual accommodations ranging from 0.4 to 1.3 D were found with both drugs even when careful single instillations of 0.075 cc were made, but the average residual accommodation with dibutoline sulfate was 0.62 D, as compared with 1.08 D with homatropine hydrobromide. The 48 eyes required an average of 0.03 D more plus sphere with the new drug than with homatropine. The difference in the astigmatic correction was insignificant.

The onset and duration of action of dibutoline were compared with the corresponding effects of homatropine on the eyes of more than 100 patients. One drop of a 5 per cent aqueous solution of dibutoline sulfate instilled into the conjunctival sac usually produced mydriasis and cycloplegia beginning in twelve to twenty minutes and becoming maximal in forty to fifty-five minutes. The onset of its effect usually preceded that of the effects of an equal dose of homatropine by ten to fifteen minutes (fig 2). The effects of the new drug on the intraocular muscles remained maximal for approximately three to five hours and nearly maximal for an additional three to eight hours and then wore off rapidly and completely within eight to ten hours. The average emmetropic young adult receiving the new drug was able to read in sixteen to twenty hours, and the near point of accommodation returned to normal in eighteen to twenty-four hours. With two instillations at five to ten minute intervals the duration averaged several hours longer. Cycloplegia produced by homatropine hydrobromide remained maximal for a shorter period, but wore off more gradually and over a considerably longer period, than an equivalent degree of cycloplegia produced by dibutoline (fig 3). When equal degrees of cycloplegia had been produced by the drugs, patients usually noticed little difference in the

period required to regain ability to read ordinary newsprint with effort, but reported that a longer period was required for their near vision to return completely to normal after homatropine was used. Mydriasis and hypersensitivity to light produced by homatropine persisted considerably longer than the corresponding effects of doses of dibutoline producing a comparable degree of cycloplegia. The pupil and the pupillary reflexes usually did not return to normal for thirty-six to forty-eight hours after instillation of 5 per cent homatropine hydrobromide which reduced accommodative power to less than 1.25 D. The visual disability produced by atropine and scopolamine lasted three to ten times as long as that produced by dibutoline.

The new drug did not influence the intraocular tension in 25 normal adults, varying in age from 20 to 78 years, however, the drug produced

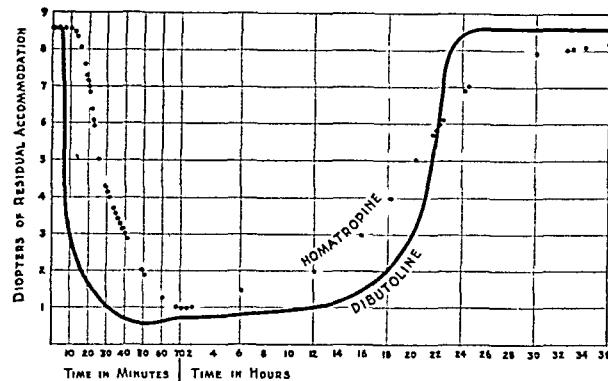


Fig 3.—Onset and duration of comparable degrees of cycloplegia produced by 5 per cent solutions of dibutoline sulfate and of homatropine hydrobromide. The values express averages for 10 young adults.

a rise in intraocular pressure in 3 patients with suspected incipient glaucoma simplex. The average maximal rise in tension produced by single instillations of a 5 per cent solution of dibutoline sulfate was 6.3 mm (Schiotz), as compared with an average rise of 8.6 mm produced in the same 6 eyes by single instillations of a 5 per cent solution of homatropine hydrobromide. The increased intraocular pressure produced by the new drug lasted an average of fourteen hours as compared with a duration of twenty-two hours for homatropine. The series of patients is too small to permit conclusions, but the results suggest that there is less danger of a rise in intraocular pressure with the new drug than with homatropine. Possibly the vasodilation produced by homatropine contributed to the higher and more prolonged increase in tension. Congestion of the conjunctival and episcleral vessels was always more pronounced in the eyes receiv-

ing homatropine than in the eyes receiving dibutoline (fig 4)

Most patients find that a single instillation of a fresh solution of 5 per cent homatropine hydrobromide in distilled water is more irritating than that of a 5 per cent aqueous solution of dibutoline sulfate, although buffered (p_H 6.5) solutions of the homatropine salt are generally described as slightly less irritating. One or two instillations at five to ten minute intervals of a 5 per cent aqueous solution of dibutoline sulfate are well tolerated, but frequent repeated instillations create conjunctival irritation and the transitory punctate disturbances of the corneal epithelium characteristically produced by surface-active drugs.³ These changes are perceptible only on biomicroscopic examination and do not interfere with refraction or with ophthalmoscopic examination. On the other hand, surface-active drugs not only penetrate the cornea

line has been used satisfactorily as a substitute for drugs of the atropine series in a case of recurrent iridocyclitis in which the patient had acquired a contact type of sensitivity to the entire atropine series of drugs.

A single instillation of a 5 per cent solution of homatropine hydrobromide is most commonly used for routine cycloplegic refraction and internal examination of the eye. For purposes of comparison, a 5 per cent solution of dibutoline sulfate was used in the studies just described. It is probable that two or three instillations of a weaker concentration of the drug will prove to be more practical than a single instillation of the 5 per cent solution. It has been our experience that the 1 drop method of inducing cycloplegia is not dependable.

The use of dibutoline as a substitute for atropine or scopolamine in the treatment of infections of the anterior segment and for the



Fig 4—Comparative effects of 5 per cent solutions of dibutoline sulfate (right eye) and homatropine hydrobromide (left eye) on the conjunctival and episcleral vessels. Photograph with a blue-sensitive film.

rapidly and consistently but facilitate penetration of other drugs. Rapid and consistent absorption is particularly desirable in a drug used for cycloplegic refraction.

A 5 per cent solution of dibutoline sulfate was instilled into the conjunctival sacs of rabbits two to three times daily for periods up to four months and into those of several patients for four to six weeks. Evidences of injury to the eye other than the transitory punctate disturbance of the corneal epithelium just described were not observed by biomicroscopic or histologic methods. No evidences of hypersensitivity, idiosyncrasy or the contact type of dermatitis and conjunctivitis were noted. The series of patients and animals studied was too small to permit conclusions but it is noteworthy that definite allergic reactions to choline esters have not been reported, while local and systemic hypersensitivity reactions to the atropine series, particularly to atropine, are not uncommon. Already dibuto-

line has been used satisfactorily as a substitute for drugs of the atropine series in a case of recurrent iridocyclitis in which the patient had acquired a contact type of sensitivity to the entire atropine series of drugs. The use of dibutoline as a substitute for atropine or scopolamine in the treatment of infections of the anterior segment and for the relief of postoperative inflammatory conditions will be the basis of a subsequent report. Preliminary investigations indicate that for these purposes the new drug has advantages over atropine and scopolamine. Dibutoline has potent antiseptic action against the organisms which commonly cause ocular inflammation, moreover, the antibacterial action of dibutoline is synergistic with that of the mercurial antiseptics. The combined use of the two substances has proved effective in the treatment of experimental inflammatory processes of the anterior segment induced in the rabbit eye by intracorneal injections of pyogenic organisms. Also, dibutoline, like other surface-active compounds, facilitates corneal penetration of the sulfonamide compounds. The duration of maximal action of dibutoline is ideal for the treatment of inflammatory conditions of the anterior segment. Its maximal mydriatic and cycloplegic action may be maintained by two to four instillations daily, yet the effects of the drug wear off in twenty-four hours after its instillation is discontinued. In contrast, the

³ Swan, K. C. Reactivity of the Ocular Tissues to Wetting Agents, *Am J Ophth* 27:1118 (Oct.) 1944.

effects of atropine and scopolamine last for days and are not readily counteracted

To provide simple mydriasis for funduscopy examination, drugs like ephedrine and eucatropine, which produce little disturbance of accommodation, are more satisfactory than dibutoline. Mydriasis produced by dibutoline is always accompanied by cycloplegia.

Some of the new drugs which we have synthesized act synergistically with atropine on the intraocular muscles.²¹ Dibutoline does not have this action, but it does facilitate corneal penetration of atropine and thereby increases the effectiveness of the latter. There is another reason that the use of dibutoline in combination with one of the atropine series may prove more desirable than administration of either drug alone, that is, patients who are relatively refractory to dibutoline seem to respond promptly to the atropine series and vice versa. Several such patients were observed.

The systemic pharmacology and toxicology of dibutoline will be reported on separately, however, it is noteworthy that the minimal lethal dose of dibutoline sulfate administered intraperitoneally in rabbits and rats is approximately 75 mg per kilogram of body weight. The minimal lethal dose by oral administration is considerably larger, so that the danger of systemic poisoning from the instillation of dibutoline into the conjunctival sac is nil as compared with that for any drug of the atropine series. The systemic action of the new drug is characterized by an antispasmodic action on smooth muscle. Depression of the salivary secretion, effects on the central nervous system and vasomotor disturbances, such as are produced by atropine and scopolamine, do not result from dibutoline. The dose of dibutoline administered to the eye is limited by the local irritation resulting from its surface activity, rather than by the danger of systemic poisoning.

SUMMARY AND CONCLUSIONS

The first substitutes for the atropine series of drugs effective on the eye have been synthesized by us. Dibutoline sulfate is the most useful member of the new class. In duration its effects are comparable to those produced by homatropine, but it is a more potent cycloplegic than the latter. Dibutoline does not produce paresis of the dilator fibers of the iris, therefore its mydriatic action may be enhanced by administration of epinephrine and related drugs. As a substitute for the atropine series of drugs in routine cycloplegic refraction and in internal examination of the eye, dibutoline has several advantages,

notably, rapid action, a short period of visual disability and negligible systemic effects from ocular administration. Unlike the atropine series, the new drug has equal effects on the iris and the ciliary body, consequently, the size and reaction of the pupil provide a convenient indication of the degree of cycloplegia. Dibutoline has an antiseptic action, which may prove advantageous in the treatment of inflammatory conditions of the anterior segment. Its duration of action is ideal for the treatment of such processes, it also facilitates penetration of other drugs.

Dibutoline has the disadvantage that repeated instillations produce irritation of the conjunctiva and a mild, transitory, superficial punctate disturbance of the corneal epithelium. These effects are due to the surface activity of the drug.

ABSTRACT OF DISCUSSION

DR S JUDD BEACH, Portland, Maine. The synthesis of a new series of mydriatic and cycloplegic drugs unrelated to atropine is a major event. Dr Swan has afforded me a short trial of dibutoline. My cases are too few to warrant my drawing any conclusions, but I wish to discuss two points in his report concerning the use of dibutoline in refraction.

Much of the recent work on cycloplegia has been unconvincing because of questionable measurement of accommodation, while none of the tests are entirely satisfactory. The authors have adhered to the classic near point test, which is probably the most effective. The value of this test lies in the response of accommodation evoked by the approach of the test object to the eye. The authors have, moreover, used test type, which appears to be better adapted to clinical examination than other symbols, such as the Duane line.

This test can be made even more exact by use of finer type than the 0.5 print, which, as the name implies, is easily read at 0.5 meter, or 20 inches, and is probably the size of type in common use for this purpose. At 20 inches the variation of 1 inch (2.5 cm) in estimation of the near point is negligible, an error of less than $\frac{1}{4}$ D being introduced, but if sufficient accommodation persists to permit the test type's being brought within 6 or 8 inches (15 or 17 cm) of the eye then the variation of 1 inch introduces an error more nearly of 2 D. The 0.5 print usually corresponds to the 4 point type of printers. Use of a card showing 3 point and 2 point type is considerably more accurate.

The other point refers to the statement that the 1 drop method of inducing cycloplegia is not dependable. This statement is correct except that it implies that repeated instillations are dependable. This is a natural, but unsafe, assumption. The effect of one instillation of a solution con-

taining 2 per cent homatropine hydrobromide and paredehyde hydrobromide ophthalmic 1 per cent with boric acid is cycloplegia which reaches its peak in forty-five to sixty minutes It then recedes slowly

In dozens of my cases it has been shown that further repeated instillations of 2 per cent homatropine hydrobromide in the regular way not only cannot be relied on to increase the cycloplegia but frequently are followed by the same slow recession, just as though no additional homatropine had been administered

I should not be surprised if dibutoline turns out to differ from homatropine in that a second instillation regularly intensifies the cycloplegia It is not the eyes that yield easily to cycloplegia but the eyes that resist which constitute the real test of potency of a cycloplegic drug I have not seen many patients presenting this problem in the past few weeks The results with the patients I have examined do not confirm the observation that dibutoline is a more potent cycloplegic than homatropine It has usually seemed that one instillation of the solution of homatropine and paredehyde hydrobromide ophthalmic is more dependable than two instillations of dibutoline sulfate yet not much weight can be given to such a small number of observations as I have made

There are other problems Does instillation of 1 drop of a solution of homatropine hydrobromide and paredehyde hydrobromide ophthalmic following instillation of dibutoline sulfate intensify the action more than a second instillation of dibutoline sulfate? I suspect it does Does dibutoline intensify the cycloplegia after homatropine has been instilled? The authors suggest that the two drugs be combined

This study seems the most ingenious and promising contribution to cycloplegia in recent years The merits of the new cycloplegic seem to be increased safety, greater speed of action and of recovery and lack of annoyance to the patients

DR JONAS S FRIEDENWALD, Baltimore This development of a new group of cycloplegics is a brilliant achievement Dr Swan's reports seem to be extremely conservative, like him, I should wish more extensive use of the drug before its full value can be determined All eagerly await further reports of its action, on the basis of which one can determine for what particular conditions the use of dibutoline has advantages equal, superior or inferior to those of the atropine series

There are, however, patients who already can be said to have been greatly benefited by this drug, namely, patients who have acquired hypersensitivity to the atropine series and treatment of whose condition is hopeless without this drug I was able to test this drug on such a patient In spite of his being hypersensitive to scopo-

lamine and similar drugs, he tolerated dibutoline well, and I produced mydriasis in his inflamed iris, which I had not been able to do for several weeks, owing to the contraindication to the use of atropine

DR WILLIAM H CRISP, Denver Every ophthalmologist must have felt at times that he would like to hear of a new cycloplegic which would overcome all the difficulties experienced with the old drugs Apparently, dibutoline sulfate is not entirely free from toxic effects, and I am afraid that there are apt to be objections to any new synthetic compound

Unfortunately, some of the experimental timing in handling a drug of this kind cannot be repeated in ordinary busy office practice I work as nearly as possible on the appointment system, but I usually drag behind in the course of a busy day, with many interruptions The result is that I have to fear some loss of efficiency of homatropine

To eliminate the toxic factor in the use of a cycloplegic, I try to make sure that the drug is instilled shortly after a fairly substantial meal, so that there is food in the stomach when the drug trickles through the nose and the nasopharynx and down into the stomach I avoid a good deal of disturbance in that way

Apart from its toxic qualities and the rather long period required for recovery, scopolamine is a valuable cycloplegic For refraction I use the drug only in my office, always watching carefully for the possibility of a troublesome reaction I have been surprised at times at the precision of its action in a young person with normally active accommodation after a single instillation of a 1:500 solution of the hydrobromide Frequently, after one instillation of the drug, with a wait of not less than an hour, the patient has promptly rejected the addition of a — ½ D sphere to a plus sphere with which I seemed to have worked out the accurate correction at the trial case

In using atropine for refraction, I do not use quite so strong a solution as some ophthalmologists With children I try to have it used six times immediately after mealtime for two days prior to my examination in a strength of 1:240, i.e. 1 grain (0.065 Gm) in 4 fluidrachms, or ½ grain (0.032 Gm) in 2 fluidrachms I carefully advise the parents not so much against occlusion of the lacrimal passages as that they instil only a single drop, having already measured how much they must draw up into the dropper to get a single drop, and that they always make the instillation after a fairly substantial meal I seldom have any troublesome toxic reactions in young children

DR KENNETH C SWAN, Iowa City I sincerely appreciate the comments of the discussers,

and I hope that the drug will live up to their expectations.

Dr Beach is justified in his criticism of our use of 0.5 print. We selected this size print not because it provided a more accurate test but because it has been used in many previous studies with other cycloplegics. We wished the members of the medical profession to be able to compare our work with that of previous investigators. After hearing Dr Beach, I realize that we erred in not selecting a more accurate test.

Dibutoline and the atropine series do not have a true synergistic action on the intraocular muscles, however, there is an apparent synergism because the new drug, being surface active,

facilitates corneal penetration of atropine and thereby increases the concentration of the latter in the eye.

Use of the new drug in combination with drugs of the atropine series might be more satisfactory in a crowded office. As Dr Crisp mentioned, a refractionist gets behind in his work when satisfactory cycloplegia is not obtained in a patient. We have observed several patients who are refractory to homatropine but not to dibutoline and vice versa. The combination of the two drugs would eliminate many of the delays due to refractory patients.

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ESTIMATION OF UNCORRECTED VISUAL ACUITY IN MALINGERERS

MAJOR HARRY EGGERS

MEDICAL CORPS, ARMY OF THE UNITED STATES

Uncorrected visual acuity¹ is an important basis for physical classification in the Army. Consequently, some soldiers, in order to escape combat service, simulate decreased visual acuity. In civilian life, in compensation or accident cases, persons also often conceal their true visual status. It is absurd in examination of such patients to rely solely on a subject's statements as to his visual acuity. By following the routine about to be described, one may in most cases estimate with reasonable accuracy the uncorrected visual acuity of ametropic persons.

A careful retinoscopic study should be made after complete cycloplegia has been obtained. Slit lamp and ophthalmoscopic examinations should rule out opacities in the media and lesions in the fundi. Neurologic conditions that cause central scotoma are not detectable with the ophthalmoscope. The history, the circumstances surrounding the case, the perimetric and tangent screen plottings at varying distances usually all aid in establishing a diagnosis of retrobulbar neuritis, toxic amblyopia or interference with

1 Visual acuity may be said to vary inversely with the minimum visual angle. This is the angle subtended at the nodal point of the eye by the smallest resolvable image. Snellen introduced the concept that a 1 minute angle represents normal visual acuity, and he designed his test types according to the plan of having the component parts of the Roman capital letters, the lines, the spaces between the lines and the breaks all of such width as to subtend 1 minute angles at certain designated distances, while the letters as a whole are enclosed in squares the sides of which subtend 5 minute angles at the same distances.

The tangent of an angle of 1 minute is 0.00029. Therefore the width of the lines, spaces and breaks of the letters on the 20 foot (6 meter) line should equal 20×0.00029 , or 0.0058 foot (6×0.00029 , or 0.00174 meter). At greater distances the widths must increase by the same ratio as that between the greater distance and 20 feet. Thus, at 100 feet (30 meters) a 1 minute angle is subtended by $100/20 \times 0.0058$ foot, or by a width of 0.029 foot ($30/6 \times 0.00174$ meter, or by a width of 0.0087 meter).

Disease of the eye, disease of the visual nerve paths and errors of refraction all decrease visual acuity and increase the minimum visual angle. Up to about 5 degrees, in natural trigonometric functions, the value of the tangent increases directly and in the same ratio as the angle. Thus, if at 20 feet a person cannot see more than the 40 foot (12 meter) letters, his minimum visual angle is 2 minutes.

the visual pathways. In the case of a soldier, the visual requirements of the occupation that was followed before induction should be considered. Further, it is unlikely that a person of fair intelligence who rather suddenly became amblyopic would have failed to seek immediate medical aid and have waited until induction into the Army or overseas service became imminent before establishing the existence of the visual defect.

The malingerer is apt to do unphysiologic things. He frequently affects photophobia, usually of an intense form. He is likely to narrow the palpebral fissures and blink rapidly. Sometimes he affects difficulty in walking about in dim illumination, despite the fact that perimetric examination may have revealed normal peripheral fields. Invariably, he overplays his part. He simulates a decreased visual acuity which is far below a reasonable correlation with the refractive error.

Occasionally it is possible to trick a simulator of poor visual acuity into conceding somewhat better vision than he had intended to admit by allowing him to see only test charts which start with smaller letters than the conventional size for the 200 feet (60 meter) distance. Repeated examinations in different rooms at different distances and with different charts and projectors also may confuse the malingerer.

The best possible correction for the refractive error should be estimated from the retinoscopic examination and from the power of the correction that is being worn. It must be remembered that some malingererers will deliberately wear lenses that are too strong. Subjective aid usually can be obtained from the examinee. Most simulators, while under the effects of a cycloplegic, can be coaxed, argued or ordered into stating whether, for the size of letter that they admit seeing, a lens is better or worse, whether it makes the letters appear straighter or more tilted, smaller or larger, and so on. In this way a fairly accurate approximation of the true correction can be obtained. A lens combination that is approximately correct for test letters which subtend a large visual angle is also approximately correct for letters at the true minimum visual angle. In young persons (under 30)

TABLE I.—Correlations of Visual Acuity and Required Connection.

Uncon- scious Visual Acuity Chart		Required Dioptric Powers of Correcting Lenses Necessary for 20/20 Vision					
Line	Value	Minus Spheres (Myopia)	Plus Cylinders (Simple Myopic Astigmatism)	Minus Spheres (Compound Myopic Astigmatism)	Plus Cylinders (Hypermetropic Astigmatism)	Minus Spheres with Plus Cylinders (Mixed Astigmatism)	Plus Cylinders (Hypermetropic Astigmatism)
20/20	-0 12 D sph	-0 20 D cyl, a\ a		-0 12 D sph, -0 25 D cyl, a\ a	-0 25 D sph, +0 50 to +0 75 D cyl, a\ a	+0 50 D cyl, a\ a	
20/20	-0 25 D sph	-0 50 D cyl, a\ a		-0 20 D sph, -0 50 D cyl, a\ a	-0 75 to -1 00 D sph, +1 00 to +1 25 D cyl	+0 75 D cyl, a\ a	
20/0	-0 97 to -0 50 D sph	-0 76 D cyl, a\ a		-0 50 D sph, -0 25 D cyl, a\ a	-0 50 to -1 20 D sph, +1 25 to +2 00 D cyl	+1 00 D cyl, a\ a	
20/10	-0 62 to -0 70 D sph	-1 00 D cyl, a\ o		-0 50 D sph, -0 75 D cyl, a\ o, or	-0 50 to -1 20 D sph, +1 25 to +2 00 D cyl	+1 25 to +1 50 D cyl, a\ o	
		-1 25 to -1 50 D cyl, a\ v or h		-0 50 D sph, -0 60 D cyl, a\ o, or	-0 50 to -1 20 D sph, +1 25 to +2 00 D cyl	+1 25 to +1 75 D cyl, a\ v	
				-0 75 D cyl, a\ v or h	-0 50 to -1 20 D sph, +1 25 to +2 00 D cyl	+1 25 to +2 00 D cyl, a\ v	
20/30	-1 00 D sph	-1 25 to -1 50 D cyl, a\ o		-0 25 D sph, -1 00 to -1 25 D cyl, a\ o, or	-0 50 to -1 75 D sph, +2 25 to +2 75 D cyl	+1 50 to +2 00 D cyl, a\ o	
		-1 75 to -2 25 D cyl, a\ v		-0 25 D sph, -1 25 to -1 75 D cyl, a\ v or h	-0 50 to -1 75 D sph, +2 25 to +2 75 D cyl	+1 75 to +2 25 D cyl, a\ v	
		-1 75 to -2 50 D cyl, a\ h		-0 50 D sph, -0 75 to -1 00 D cyl, a\ v, or	-0 50 to -1 75 D sph, +2 25 to +2 75 D cyl	+2 00 to +2 50 D cyl, a\ h	
20/10	-1 25 to -1 50 D sph	-1 75 to -2 25 D cyl, a\ o		-0 75 D sph, -0 25 to -0 50 D cyl, a\ a	-0 50 to -2 50 D sph, +2 75 to +3 25 D cyl	+2 25 to +2 50 D cyl, a\ o	
		-2 25 to -2 50 D cyl, a\ v		-0 50 D sph, -1 00 to -1 25 D cyl, a\ v, or	-0 50 to -2 50 D sph, +2 75 to +3 25 D cyl	+2 25 to +2 75 D cyl, a\ v	
		-2 25 to -2 75 D cyl, a\ h		-0 75 D sph, -1 25 to -1 75 D cyl, a\ v, or	-0 50 to -2 50 D sph, +2 75 to +3 25 D cyl	+2 50 to +3 00 D cyl, a\ h	
20/100	-1 00 to -1 75 D sph	-2 50 to -3 25 D cyl, a\ o		-0 50 D sph, -1 00 to -1 25 D cyl, a\ v, or	-0 50 to -3 00 D sph, +3 25 to +3 50 D cyl	+2 50 to +2 75 D cyl, a\ v	
		-2 75 to -3 50 D cyl, a\ v		-0 75 D sph, -1 25 to -1 75 D cyl, a\ v, or	-0 50 to -3 00 D sph, +3 25 to +3 50 D cyl	+2 75 to +3 25 D cyl, a\ v	
		-3 00 to -3 50 D cyl, a\ h		-0 75 D sph, -1 00 to -1 30 D cyl, a\ v, or	-0 50 to -3 00 D sph, +3 25 to +3 50 D cyl	+3 00 to +3 50 D cyl, a\ h	
20/150	-2 00 to -2 25 D sph	-3 00 to -3 25 D cyl, a\ o		-1 50 to -2 00 D cyl, a\ v or h	-1 50 to -1 00 D sph, +3 75 to +4 00 D cyl	+2 75 to +3 00 D cyl, a\ v	
		-3 25 to -3 75 D cyl, a\ v		-1 00 to -1 50 D sph, -1 50 to -2 00 D cyl, a\ v, or	-1 00 to -1 50 D sph, +3 75 to +4 00 D cyl	+3 25 to +3 75 D cyl, a\ v	
		-3 50 to -4 00 D cyl, a\ h		-1 00 to -1 50 D sph, -1 50 to -2 00 D cyl, a\ v, or	-1 00 to -1 50 D sph, +3 75 to +4 00 D cyl	+3 50 to +4 00 D cyl, a\ h	

20/200	-2.50 to -2.75 D sph	-3.50 to -3.75 D cyl, a\`v -4.00 to -4.50 D cyl, a\`v -4.00 to -4.50 D cyl, a\`h	-0.75 to -3.75 D sph $\tilde{\rightarrow}$ 1.50 to +5.25 D cyl +3.25 to +3.75 D cyl, a\`v +3.75 to +4.50 D cyl, a\`v +4.25 to +4.75 D cyl, a\`h
20/230	-3.00 to -3.25 D sph	-4.00 to -4.50 D cyl, a\`v -4.50 to -5.00 D cyl, a\`v	+1.00 to +4.00 D cyl, a\`v +1.50 to +5.00 D cyl, a\`v

Uncorrected Visual Acuity on Snellen Chart	Minus Spheres (Myopia)	Actual Visual Acuity	Required Correction	Visual Acuity Usually Associated with the Spherical Component	Visual Acuity Usually Associated with the Cylindric Component	Combined, or Additive, Effect (Compare with Actual Acuity)
20/300	-3.25 to -3.75 D sph	-4.75 to -5.25 D cyl, a\~o -5.25 to -5.75 D cyl, a\~v -6.00 to -6.25 D cyl, a\~h	-1.00 D sph (-3.50 to -4.00 D cyl, a\~o, or -3.75 to -4.50 D cyl, a\~v, or -4.25 to -4.75 D cyl, a\~h -1.75 D sph (-2.50 to -3.00 D cyl, a\~o, or -2.75 to -3.25 D cyl, a\~v, or -3.00 to -3.50 D cyl, a\~h -2.50 D sph (-1.25 to -1.50 D cyl, a\~o, or -1.50 to -2.00 D cyl, a\~v, or -1.75 to -2.25 D cyl, a\~h -3.00 D sph (-0.50 to -0.75 D cyl, a\~o, or -0.75 to -1.25 D cyl, a\~v or h	-0.75 to -1.00 D sph (-0.75 to -1.00 D cyl, a\~o, or -1.00 to -1.25 D cyl, a\~v, or -1.25 to -1.50 D cyl, a\~h -0.75 to -1.00 D sph (-0.75 to -1.00 D cyl, a\~o, or -1.00 to -1.25 D cyl, a\~v or h	-0.75 to -1.00 D sph (-0.75 to -1.00 D cyl, a\~o, or -1.00 to -1.25 D cyl, a\~v, or -1.25 to -1.50 D cyl, a\~h -0.75 to -1.00 D sph (-0.75 to -1.00 D cyl, a\~o, or -1.00 to -1.25 D cyl, a\~v or h	+5.25 to +5.75 D cyl, a\~v +5.75 to +6.00 D cyl, a\~h
20/400	-4.00 to -4.25 D sph	20/400	-4.00 D sph (-1.75 D cyl, a\~3	20/350	20/350	20/(250 + 200)
20/450	-4.50 to -4.75 D sph	20/450	-3.00 D sph (-3.50 D cyl, a\~68	20/250	20/250	20/(250 + 300)
20/500	-5.00 to -5.25 D sph	20/500	-3.00 D sph (-6.00 D cyl, a\~176	20/230	20/230	20/(400 + 50)
20/450	-5.50 to -6.00 D sph	20/450	-4.75 D sph (-1.25 D cyl, a\~124	20/400	20/400	20/(500 + 100)
20/500	-5.50 to -6.00 D sph	20/500	-5.75 D sph (-2.75 D cyl, a\~30	20/500	20/500	20/(500 + 100)

Beyond visual acuities of 20/300 there were not available sufficient cases in which high cylindric errors occurred to permit statistical correlation. The infrequent cases that were encountered approximately to the general pattern of the relation between visual acuity and correcting lens power. A few examples follow.

Beyond visual acuities of 20/300 there were not available sufficient cases in which high cylindric errors occurred to permit statistical correlation between the general pattern of the lesion and visual acuity and correcting lens power. A few examples follow

Uncorrected Visual Acuity on Snellen Chart	Minus Spheres (Myopia)
20/50	-4.00 to -4.25 D sph
20/400	-4.50 to -4.75 D sph
20/450	-5.00 to -5.25 D sph
20/500	-5.50 to -6.00 D sph
20/600	-6.25 to -6.75 D sph

* In this table, and in table 2, *a* indicates any axis, *o* the oblique axis (from 10 to 80 degrees), and *h*, the horizontal axis (from 180 to 10 degrees and from 170 to 180 degrees).

with hypermetropia the paralysis of accommodation need not be considered if the amount of hypermetropia is less than 4.5 D. Under these conditions the hypermetropia itself does not decrease visual acuity. Concomitant astigmatism decreases visual acuity in the same manner as it would in the absence of any hypermetropia.

After correcting lenses have been placed before the eyes the cover test should be used to determine the presence or absence of strabismus. Care must be taken that the examinee actually fixates the light. The cover test is worthless if the subject does not consciously follow the light all the time. Observation of the position of the image of the light on the cornea will determine this. An amblyopic eye may fixate eccentrically, and this fact will indicate that a central scotoma is present.

Strabismus is not present in all eyes with unilateral amblyopia. Therefore it is necessary to find out whether the presumably amblyopic eye is fixating the test letters. The examiner can do this by suddenly interposing a horizontal prism of 5 or 6 D before the doubtful eye while the subject, with both eyes open, is slowly reading some test types. Fusional movements of both eyes will occur if the eye behind the prism is fixating. In my experience such fixation, while the other eye has corrected vision of 20/20, indicates a correctable visual acuity of 20/40 or better. An eye with less visual acuity than this does not fixate during binocular vision if the other eye is good and therefore will not make a fusional movement under such circumstances.

It is well for the examiner to keep in mind two little known types of amblyopia. The first might be called "amblyopia of anisometropia." It is unilateral and is not accompanied by strabismus (if strabismus were present it would of course be amblyopia ex anopsia). When the refractive error of one eye is greater than that of the other by more than 2.5 D, it not infrequently happens that the more ametropic eye is found to be amblyopic.

The second type might be called "amblyopia of uncorrected ametropia." Usually it is bilateral. Uncorrected refractive errors may be accompanied by decreased visual acuity which is not immediately correctable by the wearing of proper lenses. After some time, usually several months, the visual acuity gradually will improve.

VISUAL ACUITY CORRELATIONS

If it has been established that an eye is free from visible disease and that it fixates, the uncorrected visual acuity can be estimated accurately if the approximate refractive error is

known. The accompanying tables represent correlations and deductions that have been made on the basis of over 6,000 refractions done on persons who had no reasons for withholding the truth. They were young adults of both sexes, under 30, who presented no encroachment of the upper eyelids on the pupillary area of the cornea and whose best corrected vision was 20/20 or better.

The resolving power of the eye varies somewhat from person to person. It is dependent on many factors, such as the size of the pupil, the location and curvature of the refracting elements with respect to each other, the structure of the macula and, possibly also, the structure and functional capabilities of the occipital cortex. Nevertheless, whenever a dishonest subject makes it necessary for an ophthalmic examiner to estimate the true visual acuity, the accompanying correlations will serve as a fair basis for appraisal.

It must be kept in mind that the correlations are expressed in terms of visual acuity measured by the Snellen test types (Roman capital letters). These test types are not as accurate as broken circles but are much more practicable. It is easier to guess a distorted letter than the position of the break in a blurred circle. Consequently, the visual acuity will appear slightly better with a Snellen test chart than with a chart of broken circles.

Consideration of the table of correlations reveals a number of points which deserve comment.

Eyes with astigmatism of identical amounts show small, but definite, variations in uncorrected visual acuity depending on the position of the axis of astigmatism. Astigmatism that requires the correcting cylinder in the horizontal axis (from 180 to 10 degrees and from 170 to 180 degrees) is associated with a slightly greater visual acuity than the astigmatism of equal amount which requires a correcting cylinder in the vertical axis (from 80 to 100 degrees). The latter form, in turn, is associated with a slightly greater visual acuity than the astigmatism requiring a cylinder in the oblique axis (from 10 to 80 degrees and from 100 to 170 degrees). Very likely the structure of the Snellen letters accounts for this, and with broken circles this variation probably could not be shown.

Simple myopic and simple hypermetropic astigmatism of the same amount are associated with practically identical decreases of visual acuity. Offhand, one would think that hypermetropic astigmatism should be associated with better visual acuity than myopic astigmatism. Theoretically, the hypermetrope can focus alter-

nately on the two planes of ametropia. Yet this does not seem to be the case.

A certain correspondence exists between cylindric and spherical corrections for myopia. Simple myopic astigmatism requiring a diverging cylinder in the horizontal axis is accompanied by about the same uncorrected visual acuity as simple myopia requiring a sphere of from 45 to 55 per cent of the numerical value of the cylinder. For example, the visual acuity that corresponds to an ametropia requiring a -2.50 D cylindric correction in the horizontal axis is 20/70. The same visual acuity usually corresponds to a myopia of -1.12 D ($0.45 \times 2.50 = 1.125$). Likewise, a minus cylinder in the vertical axis can be correlated with a minus

TABLE 2.—Simplified Table Showing Approximate Relation of Visual Acuity and Required Correction[†]

Uncorrected Visual Acuity on Snellen Test Chart	Power of Correcting Sphere for Myopia or Absolute Hypermetropia (D)	Required Cylindric Correction for Simple Myopic and Hypermetropic Astigmatism (D)†	
		Oblique Axis	Horizontal Axis
20/30	0.50	0.75	1.00
20/40	0.75	1.00	1.50
20/50	1.00	1.50	2.00
20/70	1.25	1.75	2.50
20/100	1.50	2.25	3.00
20/150	2.00	2.75	4.00
20/200	2.50	3.50	4.50
20/250	3.00	4.25	5.50
20/300	3.50	5.00	6.25
20/350	4.00		
20/400	4.50		
20/450	5.00		
20/500	5.50		
20/600	6.50		

* Spherical lens power may be converted into equivalent cylindric lens power, corrective for identical amounts of decreased visual acuity, by multiplying the dioptic value of the sphere by 1.4 for cylinders in the oblique axis, by 1.6 for cylinders in the vertical axis and by 2 for cylinders in the horizontal axis. For visual acuities lower than 20/150, the multiplication factor is 1.8 for cylinders in the horizontal axis.

Conversely, the corresponding spherical lens which corrects the same visual acuity as a specific cylindric lens can be obtained by multiplying the dioptic power of the cylinder by 0.50 when the axis of the cylinder is horizontal (by 0.55 when the visual acuity is less than 20/150), by 0.60 when the axis of the correcting cylinder is vertical and by 0.70 when the axis is oblique.

† Values for the vertical axis are intermediate.

sphere of about 50 to 60 per cent of the same numerical dioptic power while in the oblique axis the correspondence is about 60 to 70 per cent.

In a case of mixed astigmatism the retina lies somewhere between the two principal focal planes, and the condition may be regarded as being composed of two components—a myopic astigmatic component and a hypermetropic astigmatic component at the opposite axis. Thus, in the prescription $-x$ sph $\pm y$ cyl z axis, which is the correction for mixed astigmatism, $-x$ represents the strength of the diverging cylinder, at right angles to axis z that is required to bring

the first focal line back on the retina, and $y - x$ represents the power of the converging cylinder at z axis that will bring the second focal line forward to the retina.

Decreased visual acuity is synonymous with an increase in the minimum visual angle. If an ametropic condition, such as mixed astigmatism, represents the cumulative effect of two component conditions, the increased minimum angle resulting from the combination should equal the sum of the two minimum visual angles corresponding to the component ametropic factors. Thus if $20/a$ expresses the decreased visual acuity resulting from one of the astigmatic components, and $20/b$, the acuity resulting from the second component (both a and b must, of necessity, be greater than 20), then the resultant combined decreased visual acuity will equal $20/(a+b)$. It is permissible to compute in this manner because, as already stated in footnote 1, for the tiny angles used in measuring visual acuity, the value of the tangent increases directly, and in the same ratio, as the size of the angle. The fractional notation used in expressing visual acuity really is a representation of the ratio of the tangent of the standard 1 minute angle to the tangent of the minimum visual angle.

In order to estimate the visual acuity in cases of uncorrected mixed astigmatism, one simply separates the estimated or known correction into its two cylindric components. Then, from the table of correlations the visual acuity corresponding to each component can be obtained. These two values must be combined, as just indicated. For example, the required correction is -1.75 D sph ± 3.00 D cyl, axis 90. This is identical with a -1.75 D cyl, axis 180 combined with a $+1.25$ D cyl, axis 90. The visual acuity which corresponds to the first component is 20/50, and that which corresponds to the second component is 20/40. Combined, these two values equal 20/90, which is practically 20/100, and a reasonable estimate.

A similar method can be used for computing the approximate visual acuity in cases of compound myopic astigmatism. The spherical and the cylindric component may be estimated separately and then combined.

Hypermetropia has been mentioned already. Facultative hypermetropia, by itself, does not involve any decrease in uncorrected visual acuity. Absolute hypermetropia affects the minimum visual angle in about the same way as does myopia. For example, if there is 2 D of hypermetropia that cannot be overcome by the accommodation, the visual acuity probably is 20/150, for 1.5 D the acuity probably is 20/70.

QUEREAU-PUTNAM TROPOPHOROMETER

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The instrument here described has been designed to measure deviations of the eyes in cases of squint and heterophoria. It will measure vertical deviations in the six cardinal directions as well as horizontal deviations for distance and near vision. Its accuracy, especially in objective tests, is greater than that of any other method of which we know.

The principle employed is the movement of two light sources to describe two spheres the centers of which are substantially coincident with the centers of rotation of the eyeballs (fig 1). The two light sources are independently movable and are shielded in such a manner that a narrow beam is visible only to the eye about the center of which it travels. The light is visible to the observer as a reflex on the cornea of the eye fixing it. Each light is mounted on a movable arm which permits it to be swung beyond the limit of rotation of the eye in any direction. The visual line from a light to its corresponding eye can be considered a radius of the sphere, hence any movement of the light in any direction about the eye does not alter the distance of fixation.

The angle above or below the zero position is registered on scales at either side of the patient's head. Lateral deviations from the position of eyes front, or the zero position, are indicated on a scale at the base of the instrument. Lateral rotations of each eye are registered on the same scale. A differential scale is attached to one of the scale pointers, so that the angular difference between the visual lines may be read directly. Scales may be calibrated in arc degrees or in prism diopters.

In order that the centers of the spheres described by the lights shall coincide with the centers of rotation of the corresponding eyes, all scales are set at zero, and the adjusting screws at either side of the base are turned until the distance between the lights is the same as the interpupillary distance. Next, the chin and head rest is adjusted to move the head up or down,

or backward or forward, until an imaginary line between the arm pivots at either side of the patient's head passes approximately through the centers of rotation of the eyes.

On the base of the instrument, in front of the differential scale, are two rheostats for control of the brightness of the fixation lights. In front of these are switches and a flashing button. By means of these devices both lights may

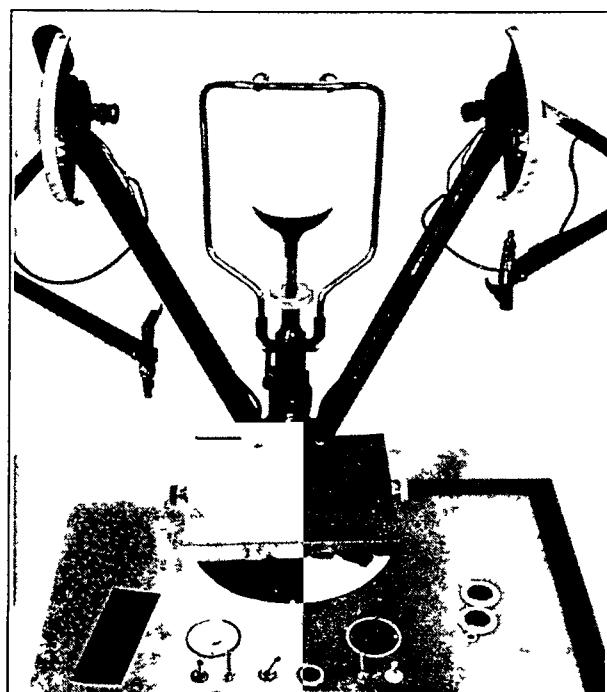


Fig 1.—Tropophorometer, showing scales and shielded lights which throw a narrow beam into the eye from the ends of the supporting arms.

be lighted continuously, either light may be left on while the other is flashed by pressing the flashing button or both lights may be flashed on and off alternately.

Both the arms supporting the lights may be shortened or lengthened. This adjustment moves the light either directly toward or directly away from the center of the eye, changing only the radius of the sphere or the distance of fixation, but not disturbing any directional relationships. Because of this provision and the fact that each light moves on a separate sphere, there is no

position in which one light will interfere with the other or will be shielded from view by it. The two lights may appear superimposed to the patient at any point in the field of binocular fixation.

With the lights placed 15 inches (38 cm) in front of the patient's eyes, an angular separation of 1 arc degree is equivalent to a linear separation of 75 mm. Most patients can detect a separation of less than 1 mm, hence a deviation of 175 mm, which represents 0.25 arc degree, or 0.5 prism diopter, is easily recognized. This accuracy of measurement is present in the entire field of fixation.

METHOD OF MEASUREMENT AT FIFTEEN INCHES

The instrument may be used in subjective determinations with the screen parallax test or the Maddox rod or red glass or simply by the examiner's asking the patient to announce when the two lights are superimposed. If larger targets are desired, polarized or chromatic shielding may be used. With polarized shielding a polarizing medium is placed in front of each target and a polarizing filter in front of each eye. The light from the two targets is polarized in planes at right angles to each other. Each filter is polarized in the same plane as the corresponding target. With chromatic shielding the targets are of complementary colors, such as red and green. A filter of the same color as the corresponding target is placed in front of each eye. With each type of shielding the right eye can see only the right target and the left eye only the left target. Objectively, the instrument may be employed with the cover test in a lighted room, and here lies its greatest field of usefulness.

The screen parallax test may best be made in a darkened room. With the two lights on and placed near each other in any part of the field of fixation, a cover is passed from one eye to the other and the position of the lights changed until the patient sees no apparent movement, just as the apparent motion of a single test object is neutralized with prisms. Instead of the use of a cover, each light may be flashed alternately.

The light directed toward the left eye is termed the left light, and the light directed toward the right eye the right light. No matter how closely the lights are brought together, the patient can see only the left light with his left eye and only the right light with the right eye. This continues to be true no matter to what degrees the visual lines cross. With the two

lights set at the same level, a patient with left hyperphoria of 2 degrees will see, on alternate flashing of the lights, what appears to be a single light which moves up and down. When the examiner moves the left eye up 2 degrees, the apparent motion will cease. The amount of deviation may be read from the vertical scales.

The Maddox rod may be used as follows. In measurement of a lateral deviation, for example, the red Maddox rod may be held in front of the left eye in a vertical position. The rays from the left light will be seen by the left eye as a vertical red line. The right eye sees only its corresponding white light, which is not visible to the left eye. The patient will now say that the red line is to the right or to the

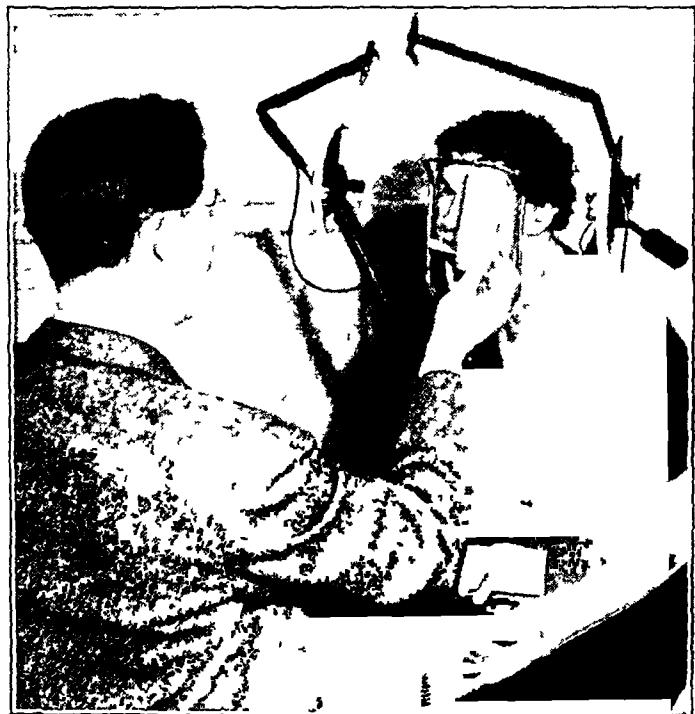


Fig 2.—Measurement of vertical deviation by the cover test with the eyes turned up 30 degrees and to the left 30 degrees. The lights have been separated 16 prism diopters laterally, the amount of the patient's exotropia for a distance of 15 inches (38 cm). The right eye can see only the right light. When the cover was shifted to the right eye, the left eye moved down to fix the left light. The left light was raised until this downward motion was neutralized, and the amount of the left hypertropia was read from the scale.

left of the light. It is necessary to move only one of the lights until the red line passes through the light. The red line may now be flashed off and on a few times to eliminate the error caused by fusion, the patient being asked to give the position of the red line when he first sees it. The amount of the deviation is read from the horizontal scale.

A dark red glass held over one eye may be employed. The patient will then see one white and one red light, each light being visible only to its corresponding eye. The examiner then moves one of the lights vertically and horizontally

until the patient sees the red light superimposed on the white light. Actually, the lights will be separated by the amount of the vertical and lateral deviation.

Objectively, the instrument may be used in conjunction with the cover test (figs 2 and 3). The cover is passed from side to side, and the movement of the eye under cover is watched as the cover is passed to the other eye. If the eye moves in to fix its corresponding light, this light is moved out until all lateral motion is neutralized. It may now be found that the covered eye moves up or down to fix its light when the cover is removed. The lights are

this way. Of course an approximate allowance for the angle alpha should be made.

METHOD OF MEASUREMENT OF DEVIATION AT TWENTY FEET

The lateral or vertical deviation for distance may be measured accurately both by the subjective and by the objective method. A 20/40 letter, cut from a vision chart, is placed at least 20 feet (6 meters) away, having been fastened to a wall with adhesive tape. The advantage of a test letter is that the patient must focus his eye for that distance in order to read it.

With the subjective method, the patient's left eye, for example, is covered, and he is asked to direct his right eye to the distant test letter. The right light is now brought to a position at which the patient sees it directly below the test letter. The light is now just below the visual line of the right eye as it fixes the distant object, and, without its lateral position's being disturbed, the light is pushed up out of view. In this way there is no distraction to the right eye, and the lateral direction of the visual line of the right eye to the distant object is precisely determined. Next, a dark red glass is placed over the patient's left eye. Through this he can see a red light but not the test letter. The left light is now moved until the patient states that it is directly under the distant letter. He is now seeing the test letter with his right eye, which cannot see the red light. His left eye sees the red light but not the test letter. The examiner extinguishes the left light by pressing the flash button, and the patient is asked to look steadily at the test letter. This permits his deviation for distance to become manifest, since the left eye is covered by the dark red glass. Then the left light is flashed on several times for only a moment and its position changed until on its first appearing the patient sees the red light superimposed on the letter. Thus the true measure of the patient's heterophoria for distance is obtained. In measurement of vertical heterophoria the same procedure is used, but the alining light is placed so that the patient sees it slightly to one side of the letter.



Fig. 3.—The lights have been moved to a point 30 degrees down and 30 degrees to the left of the position of eyes front. When the cover was moved from the right to the left eye, the right eye moved up to fix. The right light was moved down until this motion was neutralized. Left hypertropia was greatest in this field, an observation which indicated paresis of the left inferior rectus muscle.

moved vertically until this motion is neutralized, and the amount of the horizontal and vertical deviation is read from the scales. This test may be carried out in all the cardinal directions as easily as in the position of eyes front. A clear view of the eyes is afforded the examiner at all times. The corneal reflex from each light may easily be seen in a lighted room. This permits the examiner to be sure the patient is fixing properly. In addition, the angle of squint, both horizontal and vertical may be approximately measured by centering the corneal reflexes on the eye. This is helpful in the case of young children and reduces the amount of subsequent screening. Finally, the deviation of a blind eye in any direction may be measured in

In measurement of a lateral heterotropia for distance by the cover test (the objective method) the left eye, for example, is covered, and the patient is directed to look with his right eye alternately at the distant test letter and at the right light. The light is moved until the right eye does not move at all laterally in looking from the test letter to the light. Since the light can be brought to a position about 0.5 arc degree below the distant test letter without

hiding it, this light movement up and down is often unobserved. Now the right light is just below the line of fixation from the right eye to the test letter. The direction of the distant test letter having been established, the right light is extinguished or moved vertically out of view. Such vertical movement still leaves the lateral direction indicated on the horizontal scale. Next the cover is moved from side to side, and the position of the left light is changed until there is no movement when the right eye, which is fixing the distant test letter, is covered and the left eye takes up fixation of the left light. The left eye is now covered, and the patient is instructed to concentrate on the distant test letter. This permits any heterophoria or heterotropia for distance to become manifest. After a few moments the cover is suddenly shifted to the right eye, and any movement of the left eye as it again fixes the left light is noted. If movement is noted, the left light is adjusted in a direction to neutralize it and the last part of the procedure is repeated until no motion of

the left eye is observed. While the cover is being alternated from one eye to the other, any movement of the eye which is fixing the distant test letter may be disregarded, since the angle of the visual line between the right eye and the test letter has already been determined. When the change from fixation of the distant test letter with the right eye to fixation of the left light with the left eye causes no movement of the left eye, the heterophoria, or squint, for distance is read directly on the differential scale.

In measuring the vertical deviation for distance the same method is used, but the light for the right eye is aimed just beside the visual line instead of just beneath it. The light is then moved laterally out of view without the reading on the vertical scale being disturbed. The motion of the left eye is stopped by changing the position of the left light. When the movement is neutralized, the difference between the readings on the two vertical scales indicates the degree of vertical heterophoria, or squint, which exists.

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HYDROGEN ION CONCENTRATION OF THE VITREOUS IN THE LIVING EYE

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The concept of the relation of even small changes in the hydrogen ion concentration to vital biochemical and biophysical processes has stimulated many studies on the acid-base equilibrium in various body fluids and tissues. The interest of ophthalmologists has been focused mainly on one phase of this relation, that is, the changes in the turgescence of colloids due to a shift in the hydrogen ion concentration. Its possible bearing on the problem of glaucoma was considered by Fischer¹ and was later the basis for experimental work on the p_H volume curve of the vitreous (Baurmann and Thiessen,² Duke-Elder,³ Goedbloed,⁴ Salit and O'Brien,⁵ von Sallmann⁶ and others). No experimental work in ophthalmology, however, has been reported on the relation of the p_H of the milieu to the optimal action of various enzymes, such as tissue proteinases (cathepsin and peptidases).

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and the proteolytic enzymes in polymorphonuclear leukocytes and plasmacytes, whereas in other fields of medicine the problems of inflammation, autolysis and necrosis have been studied from this viewpoint (Bradley,⁷ Schade and associates,⁸ Menkin and associate,⁹ Lurie,¹⁰ Hagemann,¹¹ Steinberg and Dietz,¹² Bayerle and Borger¹³ and others). These studies have shown that accurate knowledge of the hydrogen ion concentration is of major importance in physiologic, as well as clinical, problems.

A considerable number of reports have been made on determinations of the p_H of the vitreous in experimental animals, and in a few instances in the human eye, but all the studies have been carried out on vitreous fluid removed from the eyes or on enucleated globes. As early as 1925, studies were conducted on the actual reaction of the vitreous fluid of the human eye with

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reference to glaucoma (Gala¹⁴), but in this investigation, as well as in the early experimental work on rabbits (Scalinci¹⁵), the technic was crude, as the loss of carbon dioxide was not prevented prior to the determination, the temperature factor was neglected and a colorimetric method was applied. Most of the later investigators tried to eliminate the error due to the uncontrolled loss of carbon dioxide by covering the removed vitreous with paraffin oil (Tilia and de Simone,¹⁶ Adams and Kerridge,¹⁷ de Rosa,¹⁸ Salit¹⁹ and others). The studies on the rabbit vitreous usually were carried out a short time after the death of the animal, but several hours were lost between the determination of the p_{H} of the vitreous of cattle and then slaughtered (Salit,¹⁹ Goedbloed,¹ Redslob²⁰). The small number of experiments reported by the various authors further increased the difficulty in evaluation of the results. Only Salit's investigations on the vitreous of cattle and the studies of Oyama²¹ on the vitreous of rabbits presented a sufficient number of experiments. As the technic of Oyama seems the least open to criticism from the point of view of determination of the physiologic p_{H} , it will be briefly discussed. Oyama withdrew the vitreous from the living eye of the unanesthetized rabbit into a syringe which was used as a hydrogen electrode and determined the electromotive force at a temperature of 38°C. As possible errors in the method the author mentioned the escape of carbon dioxide from the vitreous fluid into the hydrogen atmosphere of the electrode and the lowering of the partial pressure of the hydrogen gas by the escaping carbon dioxide. In addition, the filling of the needle with a small amount of a solution of sodium chloride of unknown p_{H} hydrogen ion

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concentration and the disadvantages of the hydrogen electrode, as summarized by Dole,²² must be considered in judging the readings obtained by Oyama. The hydrogen electrode was also used by Kodama,²³ Tilia and de Simone¹⁶ and de Rosa,¹⁸ but under less favorable conditions. Redslob²⁰ employed an antimony electrode in a few instances and Mayer²⁴ a gold electrode. Gala,¹⁴ Scalinci¹⁵ and Salit¹⁹ utilized colorimetric methods.

Adams and Kerridge¹⁷ were the first to apply a glass electrode to rabbit vitreous (3 experiments). It would exceed the purpose of this paper to enumerate the many advantages of the glass electrode for such determinations, the interested reader is referred to the standard text by Dole,²² who cited, among others, the following advantages:

- [1] The glass electrode comes to equilibrium immediately, allowing p_{H} measurements to be made with great rapidity.
- [2] The glass electrode can be inserted and the p_{H} measured without changing the p_{H} of the solution and without changing the solubility of gases such as carbon dioxide.
- [3] The glass electrode has no salt or protein error.

These qualities made the glass electrode suitable for the measurement of the p_{H} *in vivo* in various tissues and in different parts of the body. Voegtlín, Kahler and associates²⁵ (1932-1938) studied extensively the applicability of a new capillary glass electrode and described a technic for measuring the p_{H} of normal and malignant tissues. They also investigated the effect of the intraperitoneal injection of dextrose and fructose and the influence of severe depression of the respiration on the hydrogen ion concentration of voluntary mammalian muscle. In 1934 Ball²⁶ used

22 Dole, M. *The Glass Electrode*, New York, John Wiley & Sons, Inc., 1941

23 Kodama. *Acta soc ophth jap* **27** 489, 1923, cited by Oyama²¹

24 Mayer, L. L. *The Vitreous in Experimental Detachment of the Retina*, *Arch Ophth* **7** 884 (June) 1932

25 (a) Voegtlín, C., and Kahler, H. *The Estimation of the Hydrogen Ion Concentration of the Tissues in Living Animals*, *Science* **75** 362, 1932 (b) Voegtlín, C., Kahler, H., and Fitch, R. H. *The Action of the Parenteral Administration of Sugars on the Hydrogen Ion Concentration of Normal and Malignant Tissues in Living Animals*, *ibid* **77** 567, 1933 (c) Voegtlín, C., Fitch, R. H., Kahler, H., and Johnson, J. M. *The Hydrogen Ion Concentration of Mammalian Voluntary Muscle Under Various Conditions*, *Am J Physiol* **107** 539, 1934 (d) Voegtlín, C., Kahler, H., and Fitch, R. H. *Die Bestimmung der Wasserstoffionenkonzentration der Gewebe bei lebenden Tieren mit Hilfe der Kapillar Glaselektrode*, in Abderhalden, E. *Handbuch der biologischen Arbeitsmethoden*, Berlin, Urban & Schwarzenberg, 1938, pt 5, no 10, p 667

26 Ball, G. H. *Determination of p_{H} of Living Tissue by the Glass Electrode*, *Proc Soc Exper Biol & Med* **32** 702, 1934

a capillary glass electrode of a spear type for determination of the p_H of the intestinal wall of the white rat Dubuisson²⁷ (1936-1937) recorded the changes in the p_H which occur in the muscle during action Dusser de Barenne, McCulloch and Nims²⁸ (1937) measured the p_H of the cerebral cortex with a glass electrode of thin membrane type A technic similar to that described by Voegtlín, Kahler and Fitch^{25b} served Beck Musser, Carr and Krantz²⁹ (1938) for the measurement of the p_H of skeletal muscle and of Walker sarcoma and for the study of the effect of certain sugars on the hydrogen ion concentration of the tissue examined Maison, Orth and Lemmer³⁰ (1938) reported the changes in the hydrogen ion concentration of rabbit and human striated muscle after contraction Steinberg and Dietz,¹² in the same year, made use of the glass electrode in an investigation of the hydrogen ion concentration in relation to cell types in the inflammatory exudate of the peritoneal cavity Blank,³¹ in 1939, applied a thin membrane glass electrode to determine the p_H of the skin surface According to Dole,²² Nungerster and Kempf (1941) measured the p_H of normal and pneumonic lung tissue with a penetrating glass electrode

In application of the glass electrode for recording the p_H in various parts of the body, the following disadvantages have been found First, the friction between the electrode and the tissue caused by any slight motion may modify the reading, second, the injury of the tissue may cause a drift of potential for a certain length of time, and, third, the possible covering of the measuring membrane or capillary with blood may result in a decrease of the p_H Since these disadvantages are nearly eliminated by the semi-fluid consistency of the vitreous and its peculiar anatomy, this part of the eye seems excellently suited to the use of such an electrode Among

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31 Blank, I. H. Measurement of p_H of the Skin Surface, J Invest Dermat **2** 67 and 75, 1939

the glass electrodes designed for the work on animals, the capillary electrode of Voegtlín and Kahler^{25a} and the thin membrane electrode of MacInnes and Dole³² were most satisfactory Since the latter type of electrode permitted the measurement in a small circumscribed area of about 1 mm in diameter, a modification of this type was made and tested for the present work in the laboratory By means of such an electrode it was found possible to measure the p_H of the vitreous of rabbits *in situ* and *in vivo*

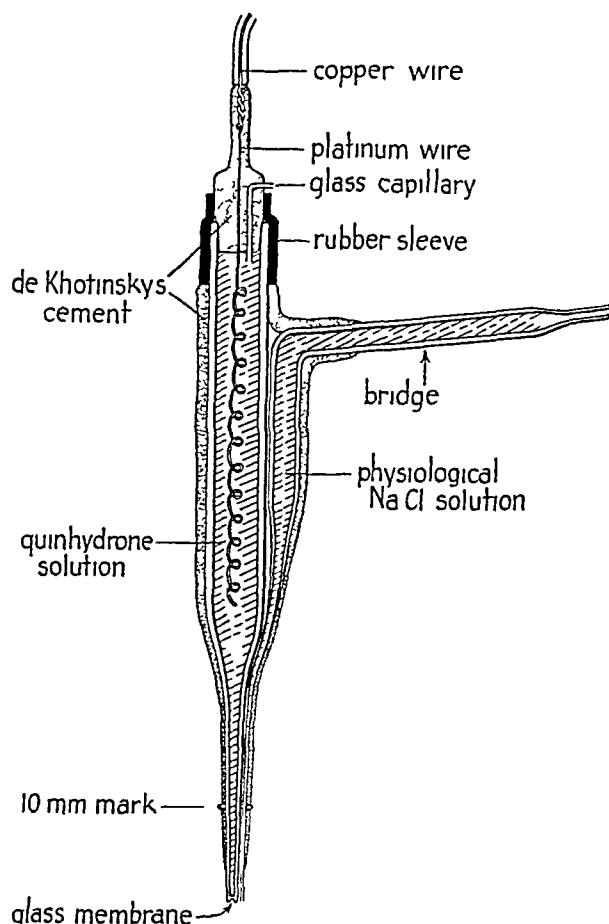


Diagram of the glass electrode which I used

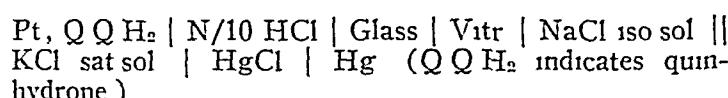
PRESENT INVESTIGATION

Preparation of Electrodes—The electrodes consisted of a tube of soft glass, one end of which was drawn out to an external diameter of 1 to 1.5 mm (figure) A thin membrane of electrode glass (Corning 015) was then welded to the fine end of the shank, according to the technic of Nims³³ The diameter of the measuring, concave membrane was about 0.5 mm To obtain the connection to the reference electrode, a glass bridge was drawn to a fine capillary, bent to the surface of the supporting tube and fixed to the latter by a layer of de Khotinsky cement This insulating material covered the electrode from its tip to its upper end to pre-

32 MacInnes, D. A., and Dole, M. Tests of a New Type of Glass Electrode, Indust & Engin Chem (Anal Ed.) **1** 57, 1929

33 Nims, L. F. Glass Electrodes and Apparatus for Direct Recording of p_H in Vivo, Yale J Biol & Med **10** 241, 1938

vent the interference by a deviation film. The openings of the capillary bridge and the measuring membrane were close to each other. A saturated solution of quinhydrone and platinum were used as the inner electrode, the platinum wire was fixed in a stopper of de Khotinsky cement, which fitted into a short rubber sleeve covering the upper end of the supporting tube. A fine opening in the cement stopper provided an air vent as a safeguard against pressure on the measuring membrane. The bridge was filled with isotonic solution of sodium chloride or of three chlorides U.S.P. to connect it with a container of the same solution, in which was immersed the calomel reference electrode. The glass electrode was held by a hard rubber clamp, which could be freely moved in various directions by a series of joints. The grounded reference electrode was held in place by a simple hard rubber clamp. The cell measured was



Leads to a Beckman p_H meter, laboratory model G, with a temperature compensator, consisted of shielded, grounded cables suspended freely in the air. The electrode assembly was arranged in an electrically shielded, grounded cage, which also contained an insulated board for the experimental animal. The potentiometer rested on a separate table and was likewise shielded and grounded to avoid the influence of extraneous electric currents. A great number of glass electrodes (several hundred) were made. After being boiled for several hours and ripened to reduce the asymmetry potential, the electrodes which gave a linear graph with three standard buffers and had a low zero correction were selected. They were recalibrated before use. A series of experiments were carried out to study the influence of the depth of immersion. It was found that the readings did not vary when the electrode was immersed in the buffer solution from 1 to 10 mm.

Technic of the Experiments.—Mature chinchilla rabbits, receiving a diet of oats and hay, were given intraperitoneal injections of sodium pentobarbital, 40 mg per kilogram, or dial with ethyl carbamate,^{33a} 1 cc per kilogram of body weight. The conjunctiva was incised a few millimeters above the limbus and the sclera exposed. The superior rectus and superior oblique muscles were resected, and the suture holding the muscle stump at the sclera was used to rotate the eye downward. An opening of 1.5 to 2 mm in diameter was made in the sclera 6 to 8 mm from the limbus. The bulging uvea was usually incised after the animal had been placed in the shielded cage and the electrode placed in position for its immediate insertion. The introduced electrode almost filled the opening and prevented the escape of vitreous. Measurements were made at various depths in the vitreous, i.e., at varying distances from the retina. Readings of the p_H were recorded three to fifteen minutes after insertion of the electrodes with the temperature compensator set at 37, 38 and 39°C. Immediately after the withdrawal of the electrode, the temperature of the vitreous was measured with a microthermometer, and in the later experiments, with a thermocouple, the wires of which were coated for the terminal 3 cm, except for the measuring tip, with a layer of de Khotinsky cement to obtain the necessary rigidity. The tip of the thermocouple was

placed in the vitreous at the same depth as the measuring membrane of the electrode. Readings were taken on the potentiometer with standard buffer solutions before and after each experiment at 37 or 38°C, the setup of the experiments being always the same. The results of experiments were tabulated only when the readings on the standard buffers after the experiment were almost exactly the same as the readings before the experiment, a slight variation of 0.02 p_H unit being allowed. The tip of the electrode and the bridge capillary were examined for traces of blood after their removal, and the eyes were dissected and examined for lesions of the lens or inner membranes and for the presence of blood in the vitreous.

RESULTS

Normal Eyes.—In 12 instances the readings for both eyes of normal chinchilla rabbits could be used (table). The results were in close agree-

Values for the p_H of the Vitreous of Normal Rabbits

Rabbit No	Values for p_H			
	With Electrode Introduced to Depth of from 5 to 7 Mm		With Electrode Introduced to Depth of from 10 to 12 Mm *	
	Right Eye	Left Eye	Right Eye	Left Eye
1	7.06	7.03	7.22 (C)	6.82 (B)
2	7.00	7.01	6.81 (B)	6.78 (B)
3	7.07	7.08	7.01	6.95
4	7.01	7.00	7.04 (C)	6.99
5	7.00	7.00	6.90	7.07 (C)
6	7.05	7.00	7.00	6.91
7	7.08	7.07	7.06	7.27 (C)
8	7.01	7.03	7.05 (D)	7.03 (A)
9	7.04	7.04		
10	7.01	7.00	7.01 (A)	7.172 (C)
11	7.05	7.03		
12	7.1	7.04	7.06	7.04 (A)
13	7.1			
14		7.00		7.04 (D)
15		7.05		7.01
16	7.01		7.12 (C)	
17		7.06		7.04
18	7.07		7.02	

* In the table, A indicates no difference between readings at different depths, B injury potential C, interference by hemorrhages and D, more alkaline readings at greater depths.

ment, the difference between comparable figures for the two eyes did not exceed 0.03 p_H unit except in 2 instances in which the differences were 0.05 and 0.06 p_H unit respectively. The values recorded for the p_H varied from 7 to 7.1, the average p_H being 7.04 at a depth of immersion of 5 to 7 mm. In the calculated average were included the results for 7 additional normal eyes, in which the fellow eye was not suitable for determinations of the p_H because of previous use or accidents during the procedure. The p_H values remained constant during the experiment, that is, for a period of fifteen minutes. Further measurements were recorded at the greater depth of 10 to 12 mm from the sclera, that is closer to the retina. The accurate loca-

^{33a} Each cubic centimeter of the anesthetic contained 0.1 Gm diallylbarbituric acid, 0.4 Gm ethyl carbamate, 0.4 Gm monoethylurea and distilled water, to make 1 cc.

tion of the electrode tip with reference to the lens and retina could not be controlled. In this position of the electrode a slight shift of the p_H to the acid side, with a range of 0.01 to 0.13 p_H unit, was noted in 11 eyes, the average shift being 0.054 p_H unit. In 3 eyes such a shift was not evident (*A*). In 3 eyes in which readings indicating a shift to the acid side p_H 6.78 to 6.82, were obtained with the deeply introduced electrode, a lesion of the retina or of the lens was observed on dissection of the globe, and therefore these readings may be considered as indicative of injury potentials (*B*). On the other hand, in 6 eyes for which the readings of the p_H at the greater depth were 7.04 to 7.27, hemorrhages in the cortical area of the vitreous were noted or traces of blood were observed on the measuring membrane or in the opening of the bridge capillary (*C*). The readings indicating slightly greater alkalinity with the deeper position of the electrode in 2 eyes (*D*) remained unexplained, since no traces of blood were noticed in the cortical part of the vitreous after dissection of the globes or on the tip of the electrode. Under the experimental conditions the temperature as measured by the thermocouple at depths of 5 to 12 mm showed a gradient in which 1 mm of immersion corresponded roughly to 0.1 degree C., that is, at a depth of 5 mm the temperature was about 0.5 degree C less than the temperature at a depth of 10 mm.

Comment.—The use of the glass electrode in the form selected eliminated the main error in determination of the p_H of the vitreous, namely, the loss of carbon dioxide prior to or during the procedure, since the shank of the electrode sufficiently blocked the opening in the sclera and the inner membranes. The temperature could also be evaluated much better by this means than by the methods applied by the aforementioned authors. The technic of determination of the p_H as applied to the vitreous of the living animals permitted readings at circumscribed areas within the cavity, providing information unobtainable by previously described methods.

The main objections to the technic used in the present experiments lay in the necessity for general anesthesia, the slight uncertainty of the temperature factor and the unavoidable introduction of a dilute saline bridge. A bridge filled with isotonic solution of sodium chloride or of three chlorides U.S.P. was used by Voegtlín, Kahler and Fitch,^{25d} as well as by other authors, in *in vivo* determinations of the p_H . It is accepted that the difference produced by this arrangement as compared with the results of *in*

vitro determinations is slight, less than 0.02 p_H unit if the electrode system is carefully calibrated with known standard buffer solutions under the same conditions of temperature as exist during the experiment. Nims²³ pointed out that the different values for any changes which occur during the course of such experiments can be ascertained within a few thousandths of a p_H unit. The question whether the anesthetic agent, dial or pentobarbital, used in these investigations changed the p_H of the tissue cannot be answered on the basis of the present experiments. All previous experiments *in vivo* were carried out in this way, with general anesthesia. It has been assumed by various investigators that an anesthesia of moderate degree induced with barbiturates has little influence on the p_H of the tissue or blood (Voegtlín and associates,²⁵ Dubuisson,²⁷ Dusser de Barenne and associates,²⁸ Beck and co-workers,²⁹ Maison and associates,³⁰ Nims,³³ Steinberg and Dietz¹²). It would be of advantage if the temperature of the cage in which the animal is placed could be kept constant at 37 to 38 C. The insertion of the small, insulated shank of the electrode may lower the temperature a little, as may the introduction of the thermocouple wire. But it is safe to assume that these errors are small, since the electrode was immersed prior to the experiment in a buffer solution at 38 C. The complicated character of the measuring system makes one cautious, however, in the statement that the readings obtained present the true physiologic p_H of the rabbit vitreous. Nevertheless, it seems that with this method fewer errors occurred than with methods used by previous authors.

The readings of the p_H recorded in the present study compare most closely to the values obtained for the vitreous of rabbits by Tria and de Simone¹⁶ (7.01) and Kodama²³ (7.1). They are similar, also, to the values for the p_H of 7.09 to 7.2 determined by Schade and associates⁸ for normal tissue, as against an average value of 7.35 for the blood. They deviate considerably from the values obtained by Oyama²¹ and other authors. Oyama stated that a p_H of 7.416 was physiologic for the vitreous of albino rabbits. It remains to be seen whether the technic applied, the breed of experimental animals or the diet on which they were kept can explain the difference in results.

The slightly less alkalinity often noted on deeper immersions of the electrode, that is, to a depth of from 10 to 12 mm indicates nothing more than a trend toward a more acid reaction.

at the cortex of the vitreous. It is not improbable that the high glycolytic activity of the retina, with the production of lactic acid, as discovered by Warburg, Posener and Negelein,³⁴ is related to these values for the p_H near the retinal surface. Adler³⁵ described a decline in the sugar concentration in the posterior layers of the vitreous as compared with the concentration in the anterior layers. The glycolysis of the lens, as studied by Kronfeld³⁶ and others, may also play a part in establishing an increased hydrogen ion concentration in the vitreous and a slight acid drift in the cortical region of the latter. Determinations of the p_H in well defined parts of the vitreous chamber by the technic described, however, were not accurate enough to permit convincing conclusions. The precise location of the tip of the electrode and its topical proximity to the retina or lens by means of ophthalmoscopic inspection was not possible, since the lower lid covered the cornea of the downward-rotated globe.

Pathologic Conditions—It is not known to what extent changes in the p_H of the vitreous space occur under pathologic conditions. The following series of experiments present a first attempt to study *in vivo* the shift of the p_H in eyes with an inflammatory process of bacterial origin in the early and late stages and in eyes in which the retina was destroyed in part by the systemic use of iodates. A few observations were made on globes with experimental secondary glaucoma. They were not conclusive enough to be reported.

Inflammation was produced by the intravitreal injection of 0.05 cc of a twenty-four hour broth culture of a mannitol-positive strain of *Staphylococcus aureus* in a dilution of 10^{-4} . The injected material gave a p_H of 7.85. The p_H of the vitreous was measured from twenty-four hours to three months after injection of the infective organisms. The technic employed was the same as that used in normal eyes, with the electrode

immersed to a depth of from 5 to 8 mm. After the measurement of the actual reaction and of the temperature of the vitreous in the same area, a small amount of vitreous fluid was withdrawn, and smears were made and stained with Giemsa's or Wright's solution for cytologic examination. In some instances the globes were removed and embedded for further histologic examination. The incidence of disturbing hemorrhages or injuries to the inner structures of the eye was higher in the later stages, especially in greatly shrunken globes.

Local acidosis was observed in all inflamed eyes. Twenty-four hours after the injection (4 eyes), the p_H value reached 5.7 in one eye and ranged from 6.33 to 6.35 in 3 other eyes. During the following weeks the acidosis declined slightly to an average p_H of 6.62 (7 eyes). Of 6 eyes in which the infection had been arrested by penicillin therapy and the clinical signs of inflammation had subsided, the p_H readings returned to a normal range in 3 (7.698 and 7.01) and declined to values indicating greater alkalinity in the other 3 (7.16, 7.19 and 7.22).

In the first days after the infection large numbers of cocci were seen in the smears or in the sections, and the inflammatory cells consisted almost exclusively of polymorphonuclear leukocytes. In later stages numerous macrophages were present, and the polymorphonuclear leukocytes displayed various stages of degeneration. A distinct relation between the cell type and the hydrogen ion concentration could not be established beyond the fact that maximal acidosis was recorded in the acute, early stages, when polymorphonuclear leukocytes were predominant. Further experiments are necessary to determine whether this initial acidosis is due to acid formation resulting from bacterial metabolism.

The acidity of the vitreous measured in the first weeks after the infection exceeded that observed by Steinberg and Dietz¹² in the peritoneal exudate of rats produced by staphylococcal infections, with p_H readings of 6.6 to 7.27. This range presents only a slight change as compared with the values determined for normal rats, in which a concentration of hydrogen ions of from 6.87 to 7.1 was recorded. The relatively great variations of the physiologic values for the p_H in the peritoneal cavity suggest, however, that the unknown placing of the tip of the electrode in the abdomen, the movement of the intestine, and possibly some concealed small hemorrhages, induced potential errors which could be avoided in the intravitreal measurements on rabbits.

34 Warburg, O., Posener, K., and Negelein, E. Ueber den Stoffwechsel der Carcinomzelle, Biochem Ztschr **152** 309, 1924. Warburg, O. The Metabolism of Carcinoma Cells, J. Cancer Research **9** 148, 1925, Die Milchsaurebildung beim Wachstum, Biochem Ztschr **160** 307, 1925.

35 Adler, F. H. An Investigation of the Sugar Content of the Ocular Fluids Under Normal and Abnormal Conditions and the Glycolytic Activity of the Tissues of the Eye, Tr Am Ophth Soc **28** 307, 1930, The Metabolism of the Retina. Further Notes, Arch Ophth **6** 901 (Dec) 1931.

36 Kronfeld, P. Zur Frage der Linsenatmung, Ber u. d. Versammel d. deutsch ophth Gesellsch **46** 230, 1927.

Neither Steinberg and Dietz¹² nor Lurie¹⁰ noted a correlation between the hydrogen ion concentration of an exudate and the leukocytic formula in their experiments on rats, rabbits and dogs. Contrary to the observations of these investigators, Menkin and associates⁹ had previously concluded from their extensive studies on dogs that "the cellular composition of an inflammatory exudate is a function of the concentration of the hydrogen ion in the area of inflammation." The p_H concentration of a pleural exudate shifts, according to Menkin from the alkaline to the acid p_H side after two or three days. Collateral with this change is the percental fall of polymorphonuclear leukocytes and the percental rise of mononuclear phagocytes. These observations of Menkin and associates were not corroborated by the results of the present study on one type of bacterial inflammation in the rabbit vitreous.

Schimmel and Riehm³⁷ observed, as an apparently isolated severe injury to the retina, acute pigmentary degeneration in patients who had been treated systemically with concentrated Pregl's solution of the sodium salt of hydriodic acid and iodic acid with iodine (0.04 per cent). Riehm³⁸ presented experimental proof of the toxic action of concentrated Pregl's solution on the retina of rabbits. In the period following these publications the nature of this destruction was repeatedly studied. Vito³⁹ Kalt⁴⁰ and, later, Sorsby⁴¹ found that sodium iodate ($NaIO_3$) was as effective as sodium hypoiodite ($NaIO$), which I⁴² concluded was the active principle in the concentrated Pregl solution. Because of the simpler technic, sodium iodate was used in the present experiments in order to obtain extensive destruction of the retina without primary interference with the retinal circulation.

37 Schimmel Zur Septojodbehandlung, Munchen med Wchnschr **73** 590, 1926 Riehm, W Augenschadigungen nach Septojodinjektionen, ibid **73** 590, 1926

38 Riehm, W Ueber Pressjod Schädigung des Auges, Klin Monatsbl f Augenh **78** 87, 1927

39 Vito, P Contributo allo studio della degenerazione pigmentaria della retina indotta dalla soluzione iodica di Pregl, Boll d'ocul **14** 945, 1935

40 Kalt, E De l'action novice sur l'épithelium pigmentaire de la rétine, des solutions de certains composés iodiques injectées par voie parentérale, Bull Soc d'opt de Paris **49** 304, 1937

41 Sorsby A Experimental Pigmentary Degeneration of the Retina by Sodium Iodate, Brit J Ophth **25** 58, 1941

42 von Sallmann, L Ueber Netzhautschädigung durch Salze der unterjodigen, unterbromigen und unterchlorogen Saure, Ztschr f Augenh **80** 342, 1933

Three injections of the aqueous solution, each of 0.03 Gm per kilogram of body weight, were administered subcutaneously to 4 rabbits at intervals of three days. Determination of the p_H was carried out from four weeks to four months after the first injection of the iodate solution. Two of the 8 eyes with the characteristic lesion fully developed could not be used for recording of the p_H values, in 1 instance because of injury to the lens with the electrode, and in the other because of the death of the animal before the readings on the second eye were completed. After the measurements the remaining 6 globes were enucleated for histologic examination. The average for the p_H values for the vitreous of the diseased eyes showed a decline in the hydrogen ion concentration as compared with the average for the p_H values of normal rabbit vitreous. For 3 eyes the readings were within a normal range (7.1, 7.06 and 7.07), the other 3 eyes showed a shift to the alkaline side (7.4, 7.18 and 7.25). The histologic examination suggested a relation between the extent of the retinal atrophy and the alkalinity of the vitreous so far as the more alkaline readings were obtained for the vitreous of eyes with larger areas of completely atrophic retina without any other microscopically detectable lesions. Adler³⁵ produced atrophy of the retina in 3 eyes of rabbits by section of the optic nerve back of the eyeball and observed that the sugar content of the vitreous of the eyes operated on was much above normal. He saw the most likely explanation of this observation in the reduction of the glycolysis of the atrophied retina. It is possible that the slight shift of the p_H to the alkaline side in the present experiments was also caused by interference with the glycolytic activity of the diseased retina and diminished formation of lactic acid. The possibility cannot be excluded, however, that the general condition of the experimental animal in this type of intoxication also influences the p_H of the tissue.

SUMMARY

1 A glass electrode of the thin membrane type (MacInnes and Dole) was designed for determination of the p_H in circumscribed areas of the vitreous *in vivo*. Accurate measurements of the temperature in the examined area, necessary for evaluation of the p_H readings, were obtained by the use of a thermocouple.

2 The potentiometric readings of the p_H of the two eyes of individual rabbits were in good agreement. A range in p_H of 7 to 7.10 was recorded as the value for the normal vitreous.

of rabbits. Measurements carried out in closer proximity to the retina showed in the majority of the eyes a trend toward an increase of the hydrogen ion concentration in the cortical layers of the vitreous. This shift may be the result of acid formation caused by the high glycolytic activity of the retina.

3 Local acidosis, up to a p_H of 5.7, developed in the early stages of an acute staphylococcal infection of the vitreous. The acidity decreased

during the following weeks. Several months after the inflammation had been arrested by penicillin therapy, a normal range of the p_H was restored in the vitreous or the acidity was succeeded by a slight alkalosis.

4 In eyes in which the retina had been partially destroyed by systemic treatment with sodium iodate, readings indicated a higher alkalinity than for normal eyes.

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AFTER-IMAGE PERIMETRY

A RAPID METHOD OF OBTAINING VISUAL FIELDS, PRELIMINARY REPORT

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The phenomenon of after-image has long been known and studied, but it has apparently not been utilized as a means of perimetry. It is reasonable to suppose that if an after-image were produced in a patient with a lesion of the central optic pathways, there might be a defect in the after-image corresponding to the site and size of the area of damage of the visual system. This hypothesis was tested according to the following technic.

METHOD

Technic—The instrument used consists of a portable flood lamp with a 500 watt bulb and a 16 inch (40 cm) reflector. Over the reflector is placed a translucent cover 0.5 mm in thickness, made of two layers of white broadcloth, on the surface of which a standard visual field design is sewed in black, the lines being 5 mm in width. The test is best carried out in a dark room with black or dark gray walls. This screen flood lamp is placed 20 cm directly in front of the eye to be tested, the other eye being covered with a shield. At a distance of 20 cm this 40 cm, round design represents 45 degrees of the complete visual field, being slightly smaller than the field charted as normal for a 5 mm object at a distance of 2 meters by the standard tangent screen method. With the room lights on, the patient is asked to look at the central focal point on the design and is cautioned against blinking the eye, and the flood lamp is turned on as the ceiling lights in the room are simultaneously turned off. The flood lamp is snapped off after a one second exposure, the room being left in total darkness, and the lamp is removed from in front of the patient. Soon an after-image appears, representing 45 degrees of the patient's field of vision. With the room dark, the patient perceives a positive after-image of the design, which is an exact reproduction of the white disk with black lines. The positive after-image tends to come and go, becoming fainter with each return. The patient is allowed to study the positive after-image through three or four cycles, and then the room lights are switched on and the retina restimulated. The design is immediately reproduced as a negative after-image, which the patient perceives as a design of white lines projected on the black background. This negative after-image fades rapidly, but by means of the room lights being switched off and on the after-image is each time reproduced clearly. The patient is thus enabled to study his own "visual field." A normal eye perceives the entire design, with clearcut borders, whereas the eye with an absolute field defect perceives a distinct absence in the after-

image. After studying the positive and negative after-images for approximately two minutes, the patient is able to chart his own "visual field" on a standard form, outlining any area which was not visualized in the after-image. A "control" is afforded by the use of a design with two small defects in one of the radial lines, which the patient is able to identify in the after-image.

Results—A series of 50 patients, 25 with normal fields and 25 with abnormal fields, were examined by this method and the results compared with their fields obtained by the standard tangent screen method used at the Neurological Institute of New York. All the normal subjects in this series were able to see their visual fields represented by the after-image clearly, distinctly and without question. Each subject with abnormal visual fields in the series was immediately aware of his own field defect, provided the defect was absolute and not relative, and was able to chart his own fields, which corresponded closely to the fields charted by the tangent screen method. The average time required for the patient to obtain and chart visual fields for both eyes by this method was four minutes. The fields charted by this group approximated their true fields closely enough to justify the clinical use of this method. In figures 2, 3 and 4 are shown the visual fields of 3 patients, with large field defects, scotomas and enlarged blindspots due to papilledema respectively. The tangent screen fields were obtained with a 5 and a 2 mm object on a 1 meter screen at a distance of 1 meter, with daylight illumination. The fields are charted on a 25 degree design, though they actually represent 45 degrees.

COMMENT

The advantages of this method of obtaining visual fields are as follows:

- 1 The method is not tiring to the patient or to the examiner.
- 2 The patient is unable to look away from the fixation point, since the after-image moves simultaneously with any shift of the eye.

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3 With a hand lamp the method is readily adaptable to the bed patient, who sees the after-images on the ceiling.

4 With a simple design of an object in each quadrant, the method can be utilized for children, who find the phenomenon attractive.

5 Fields can be conveniently determined daily for patients with tumor of the pituitary who

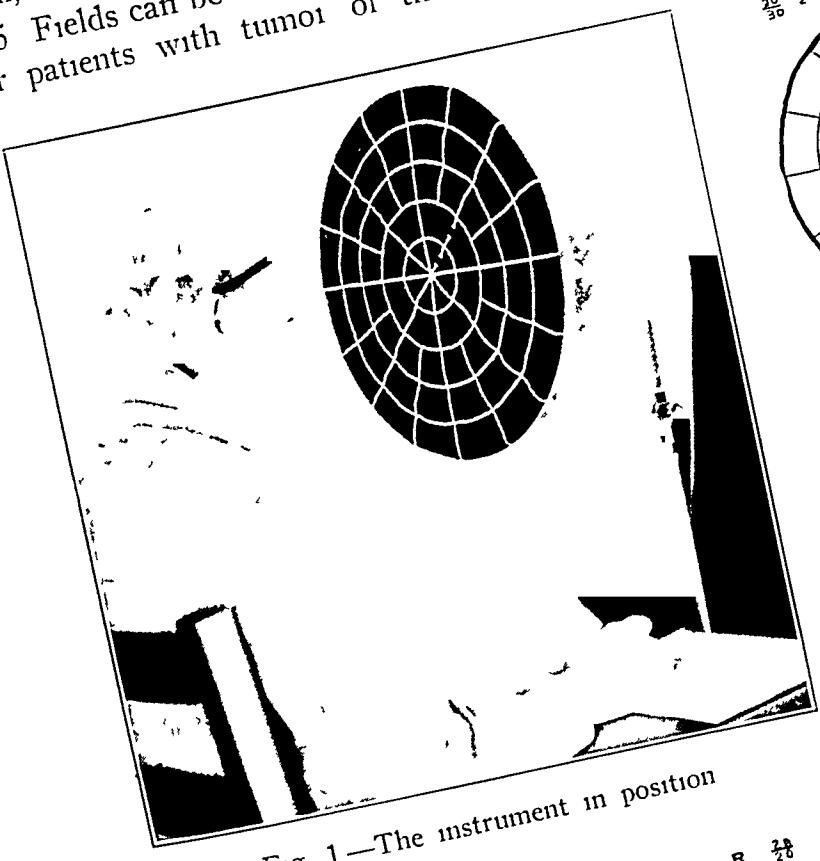


Fig 1.—The instrument in position

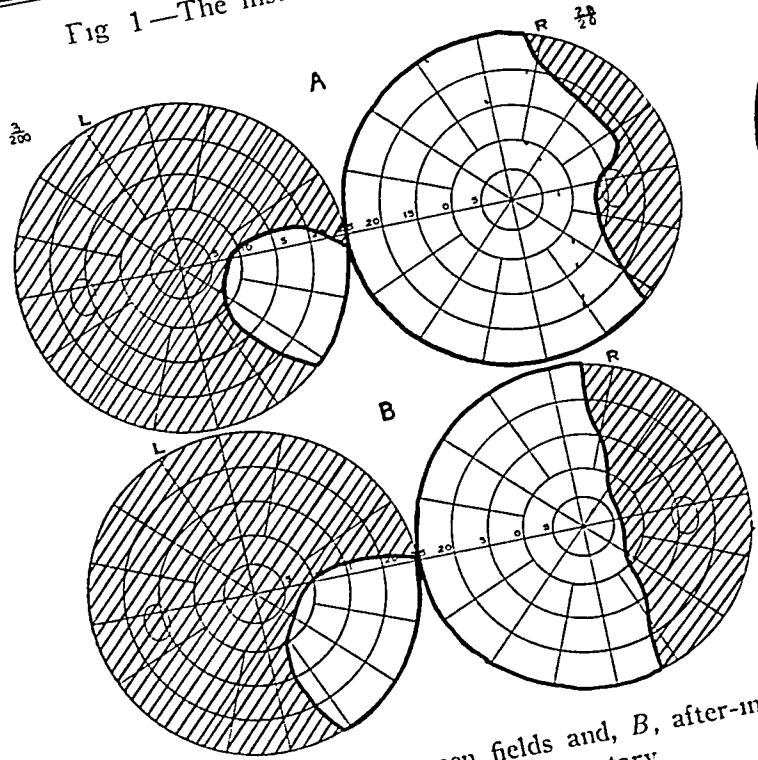


Fig 2.—A, tangent screen fields and, B, after-image fields in a case of adenoma of the pituitary

are receiving roentgen ray therapy, for patients with active multiple sclerosis with changing scotomas or for patients with any type of abnormal visual fields undergoing rapid change

6 The method is time saving, enabling one technician to increase the number of fields charted from seven to seventy or more a day.

7 It is readily adapted to the physician's office.

8 It can be utilized in "processing" methods, such as routine examinations for the armed services.

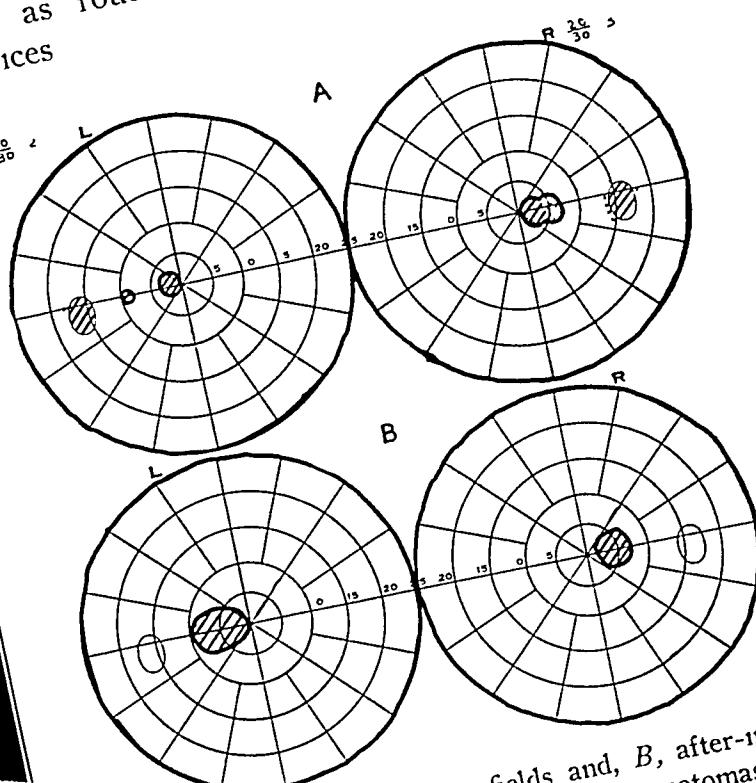


Fig 3.—A, tangent screen fields and, B, after-image fields in a case of multiple sclerosis with scotomas

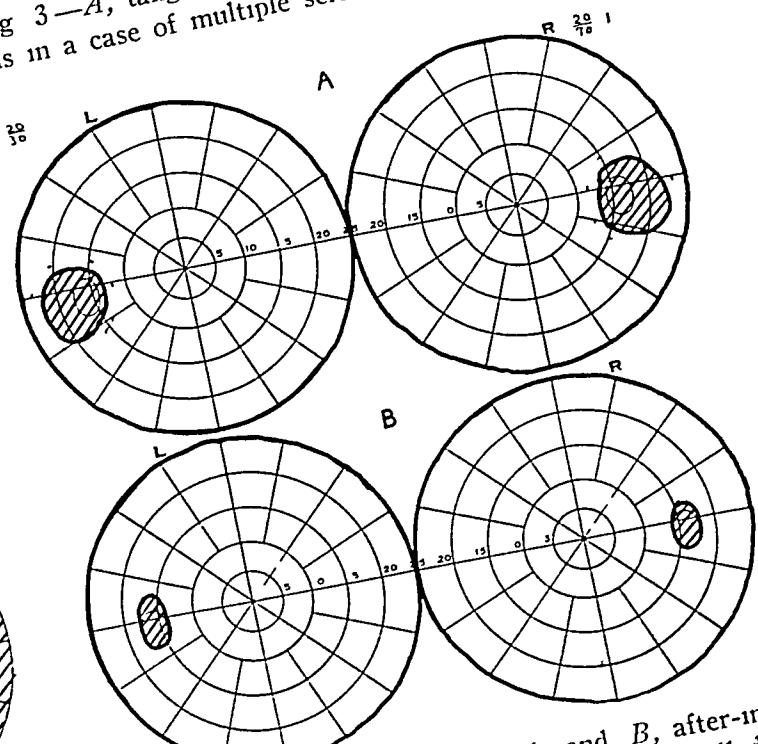


Fig 4.—A, tangent screen fields and, B, after-image fields in a case of enlarged blindspots due to papilledema

9 The apparatus is simple and easily available, since it consists only of a flood lamp and a cloth shield which any seamstress can prepare overnight.

The disadvantages of the method are as follows

1 The normal blindspot is not visualized, since it has no cortical representation. An enlarged blindspot, however, can be visualized in the after-image.

2 It will no doubt prove to be less accurate than the tangent screen method, though thus far it appears to be accurate enough for clinical use. This can be determined only after further study.

3 With the present technic the portion of the peripheral field tested does not represent more than 45 degrees.

4 The method reveals only absolute field defects.

SUMMARY

The value and limitations of this new method for determination of the visual fields are being thoroughly explored, and the results of the investigation will be published later.

Neurological Institute of New York

PENETRATION OF PENICILLIN IN RABBIT EYES WITH NORMAL, INFLAMED AND ABRADED CORNEAS

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PENETRABILITY OF PENICILLIN

Struble and Bellows¹ pointed out that in the evaluation of any chemotherapeutic agent the efficiency of the agent depends not only on its antibacterial potency but on its diffusibility and its concentration in the infected part Von Sallmann and Meyer² and Struble and Bellows¹ studied the penetration of penicillin in the normal eyes of rabbits and dogs

Von Sallmann and Meyer² were unable to demonstrate any antibacterial activity of penicillin in the aqueous humor after repeated applications of solutions and ointments containing penicillin to the normal rabbit eye, but obtained high levels of penicillin in the aqueous with the corneal bath and iontophoretic technics Struble and Bellows¹ also demonstrated high concentrations of penicillin in the aqueous humor after corneal baths of penicillin and showed that the level in the cornea exceeded the level in the aqueous when the corneal bath technic was used Subconjunctival injections also produced high concentrations of penicillin in the cornea and aqueous humor of normal rabbit eyes, the levels in the cornea again exceeding the concentrations in the aqueous humor The latter investigators, whose studies were, like the work of von Sallmann and Meyer², done entirely on normal eyes, did not report on the simple application of penicillin solution or ointment

No studies on the penetration of penicillin in eyes with inflamed or abraded corneas had been reported at the time of preparation of this paper

Read at a meeting of the College of Physicians of Philadelphia, Dec 21, 1944

From the Department of Ophthalmology, University of Pennsylvania School of Medicine

The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania

¹ Struble, G C, and Bellows, J G Studies on the Distribution of Penicillin in the Eye, *J A M A* 125 685 (July 8) 1944

² von Sallmann, L, and Meyer, K Penetration of Penicillin into the Eye, *Arch Ophth* 31 1 (Jan) 1944

It is in such eyes that penicillin will be used clinically The following studies were undertaken to determine whether or not simple applications of penicillin in the form of drops or ointment to the conjunctival cul-de-sac would give satisfactory levels in the aqueous humor and thus remove the necessity of resorting to subconjunctival injections, corneal baths or iontophoresis in the presence of corneal inflammation, for it is quite thinkable that the permeability of the pathologic cornea to penicillin is different from that of the normal cornea

Method—All the studies were made on rabbit eyes The rabbits were of a brown-eyed or blue-eyed chinchilla strain, and weighed 2 to 3 Kg each The penicillin in solution consisted of 500 Oxford units of the sodium salt per cubic centimeter of isotonic solution of sodium chloride³ The penicillin ointment was prepared with a polyethylene glycol (Carbowax) base recommended by Dr Frank Meleney through the Committee on Surgery of the National Research Council⁴ The concentration of penicillin in the ointment was 500 Oxford units per gram of base Four drops of the penicillin solution or 0.2 Gm of penicillin ointment was applied to the conjunctival sac once, and aqueous humor was withdrawn fifteen minutes, forty-five minutes or one hour and forty-five minutes after the instillation The cornea and the cul-de-sac were thoroughly washed with isotonic solution of sodium chloride, and then the cornea was anesthetized with 1 to 2 drops of 0.5 per cent tetracaine hydrochloride, after which limbal punctures were made with a sterile 27 gage needle attached to a sterile tuberculin syringe In this manner, the local anesthetic did not influence the penetration of the penicillin

The same procedure was carried out on 24 normal rabbits, 24 rabbits with inflamed corneas and 24 rabbits with mechanically denuded corneas Inflammation of the corneas was produced in 24 rabbits by intracorneal injections of 0.01 cc of a twenty-four hour broth culture containing approximately 200 organisms The organism used was *Pasteurella leptiseptica*, the ulcers produced by this organism having been previ-

³ The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council

⁴ Meleney, F F Personal communication to the authors, July 17, 1944 The Carbowax compounds are polyethylene glycols of high molecular weight The one used in these studies had a molecular weight of 4 000

ously described.⁵ The epithelium was removed from the corneas of 24 rabbits by rubbing the corneal surface with gauze, fluorescein staining serving as a guide to the amount removed. Approximately one third of each corneal surface was thus denuded.

Into 12 additional normal rabbit eyes drops of penicillin solution were instilled repeatedly every fifteen minutes for one hour. Specimens of aqueous were withdrawn from 4 eyes at each of the following intervals after the last application of penicillin fifteen minutes, forty-five minutes and one hour and forty-five minutes.

The specimens of aqueous humor from 12 normal rabbit eyes were analyzed for concentration of penicillin at fifteen minutes, forty-five minutes and one hour and forty-five minutes after an intramuscular injection of 1,500 Oxford units of penicillin per kilogram of body weight. Four eyes were used for each time interval. The same procedure was then repeated on 12 rabbit eyes with corneal inflammations caused by intracorneal injections of Past leptiseptica.

All concentrations of penicillin in the aqueous humor were determined by the bioassay method of Holmes and Lockwood.⁶ This method was satisfactory in our hands for levels above 0.02 unit per cubic centimeter.⁷ The error in this biologic method is approximately 20 per cent.

TABLE 1—Concentrations of Penicillin in the Aqueous Humor Obtained by Local Instillation of Penicillin in Solution and in Ointment Vehicles*

Time of Aqueous Humor Puncture after Instillation of Penicillin, Min	Eyes with Normal Cornea			Eyes with Inflamed Cornea		Eyes with Abraded Cornea	
	Solution Oxford Units per Cc	Ointment, Oxford Units per Cc	Repeated Instillation of Solution † Oxford Units per Cc	Solution Oxford Units per Cc	Ointment Oxford Units per Cc	Solution Oxford Units per Cc	Ointment Oxford Units per Cc
15	0	0	0	0.5	0.5	1.5	0.6
45	0	0	0	0.5	0.8	1.5	0.6
105	0	0	0	0.4	0.4	0.6	0.4

* The concentration at each time interval represents the average for 8 eyes except for the values for repeated instillations of the solution in these tests 4 eyes were used for each time interval.

† The instillation of the solution was repeated every fifteen minutes for four doses.

TABLE 2—Concentration of Penicillin in the Aqueous Humor Produced by Intramuscular Administration of 1,500 Oxford Units of Penicillin Per Kilogram of Body Weight*

Time of Aqueous Humor Puncture after Adminis- tration of Penicillin, Min	Eyes with Normal Cornea, Oxford Units per Cc	Eyes with Corneal Inflammation Oxford Units per Cc
15	0	0.4
45	0	0.15
105	0	0.15

* Each concentration obtained represents the average for 4 eyes.

Results—The results are tabulated in tables 1 and 2. Each value recorded represents the average for 4 or 8 eyes and is so specified in

5 Leopold I H, Holmes, L, and LaMotte, W O, Jr. Local Versus Systemic Penicillin Therapy of Rabbit Corneal Ulcers Produced by Gram-Negative Rod, Arch Ophth 32:193 (Sept) 1944.

6 Holmes, L, and Lockwood, J. Studies on Bioassay of Penicillin, Am J M Sc 207:267 (Feb) 1944.

7 Bioassays were done in the Harrison Department of Surgical Research University of Pennsylvania, with the assistance of Dr Lida F Holmes.

each instance. It is evident from these results that instillation of penicillin in drops or as an ointment, even when repeated four times an hour, fails to produce detectable concentrations of the substance in the aqueous of the normal rabbit eye. This confirms the observation of von Sallmann and Meyer.² However, definite concentrations of penicillin in the aqueous humor could be obtained after only one application of solution or ointment to rabbit eyes with inflamed or denuded corneas. All levels of penicillin in the aqueous humor of such eyes were above 0.2 Oxford unit per cubic centimeter one hour and forty-five minutes after a single instillation of either drops or ointment. From the results recorded in table 2 it is evident that intramuscularly administered penicillin does not penetrate readily into the aqueous humor of the normal rabbit eye but that it does penetrate readily into the aqueous of the rabbit eye with an inflamed cornea.

TABLE 1—Concentrations of Penicillin in the Aqueous Humor Obtained by Local Instillation of Penicillin in Solution and in Ointment Vehicles*

Time of Aqueous Humor Puncture after Instillation of Penicillin, Min	Eyes with Normal Cornea			Eyes with Inflamed Cornea		Eyes with Abraded Cornea	
	Solution Oxford Units per Cc	Ointment, Oxford Units per Cc	Repeated Instillation of Solution † Oxford Units per Cc	Solution Oxford Units per Cc	Ointment Oxford Units per Cc	Solution Oxford Units per Cc	Ointment Oxford Units per Cc
15	0	0	0	0.5	0.5	1.5	0.6
45	0	0	0	0.5	0.8	1.5	0.6
105	0	0	0	0.4	0.4	0.6	0.4

Comment—Rammelkamp and Keefer⁸ showed that the concentration of penicillin in serum required for maximum bacteriostatic effect against *Streptococcus haemolyticus* is 0.019 unit per cubic centimeter and that 0.15 unit per cubic centimeter produces maximum bacteriostasis against *Staphylococcus aureus*. It is evident from the concentrations in the aqueous recorded here that this necessary antibacterial concentration is exceeded for a period of one hour and forty-five minutes after one application of solution or ointment containing penicillin in eyes with loss of the corneal epithelium barrier or with corneal infections. This indicates that repeated instillation of the drops or ointment once every two hours in such eyes would maintain adequate levels of penicillin in the aqueous humor.

Struble and Bellows¹ showed that the levels in the cornea always exceed the levels in the

8 Rammelkamp, C H, and Keefer, C S. Absorption, Excretion and Distribution of Penicillin, J Clin Investigation 22:425 (May) 1943.

aqueous humor when the penicillin is applied locally. They also showed that the concentration in the cornea is less than that in the aqueous humor when the penicillin is given intravenously. It follows, therefore, that the concentration of penicillin in the cornea was probably greater than that in the aqueous in each instance in the present study in which penicillin was used locally. It has been demonstrated experimentally⁵ that local penicillin therapy is superior to intramuscular therapy for corneal inflammations. The present studies on penetration of penicillin also indicate that local application is superior to parenteral administration of penicillin in obtaining high concentrations in the cornea. One can conclude from these studies that it is not necessary to resort to iontophoresis or to the corneal bath technic in order to obtain satisfactory levels of penicillin in the aqueous humor when the corneas have been denuded or are infected. The simple instillation of drops of solution containing 500 Oxford units of penicillin per cubic centimeter or the application of penicillin ointment will give satisfactory levels in the aqueous humor in such eyes.

This increased intraocular penetration of locally and of parenterally administered penicillin in eyes with pathologic corneas over that observed in eyes with normal corneas has been noted similarly for the sulfonamide compounds.⁹

EFFECTS OF THERAPEUTIC CONCENTRATIONS

It is essential to determine the local toxic effects of any new agent before recommending its repeated local use in the eye. The experiments of Florey and associates¹⁰ on tissue cultures and the studies of Thygeson on leukocytes, cited by Hobby and associates,¹¹ indicated that little if any toxic effects on the corneal epithelium should be expected from penicillin. Von Sallmann,¹² however, showed that corneal baths with concentrations of 0.5 to 1 per cent of peni-

9 Gallardo, E., and Thompson, R. Sulfonamide Content of Aqueous Humor Following Conjunctival Application of Drug Powders, *Am J Ophthalmol* **25** 1210 (Oct) 1942 Scheie, H. G., and Leopold, I. H. Penetration of Sulfathiazole into the Eye, *Arch Ophthalmol* **27** 997 (May) 1942 Leopold, I. H., and Scheie, H. G. Studies with Microcrystalline Sulfathiazole, *ibid* **29** 811 (May) 1943

10 Abraham, E. P., Florey, H. W., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., and Jennings, M. A. Further Observations on Penicillin, *Lancet* **2** 177 (Aug 16) 1941

11 Hobby, G. L., Meyer, K., and Chaffee, E. Chemotherapeutic Activity of Penicillin, *Proc Soc Exper Biol & Med* **50** 285 (June) 1942

12 von Sallmann, L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with *Pneumococcus*, *Arch Ophthalmol* **30** 426 (Oct) 1943

cillin (sodium salts, pH 7 to 8) damaged the corneal epithelium and the superficial stroma. This damage of the corneal epithelium produced by high concentrations of penicillin in solution may account for the high concentration of penicillin in the aqueous humor obtained by the corneal bath technic of Struble and Bellows.¹ Von Sallmann² also disclosed that a concentration of 0.25 per cent of the penicillin salt produced corneal damage when applied by iontophoresis but not as a corneal bath. A concentration of 0.1 per cent of sodium penicillin produced little or no corneal damage in his hands, even when applied by iontophoresis.

Of the several factors which must be considered in determination of the toxicity of any compound to be applied locally to the eyes, the concentration of the agent and the frequency of application are important. The studies of von Sallmann¹² indicated the upper limits of concentration. The purpose of the present experiment was to determine the influence of repeated applications of a therapeutically effective concentration of penicillin on the regeneration of corneal epithelium.

Method—Twelve rabbits were used in this series, all of a blue-eyed chinchilla strain and weighing between 2 and 3 Kg. The corneal epithelium was removed from the entire cornea of each of the 24 eyes. Previous experiments have shown that eyes with denudation involving the limbus are more likely to show retardation of epithelial regeneration from chemotherapeutic agents than are eyes with central denudations not involving the limbus.¹³ All the eyes were anesthetized with 0.5 per cent tetracaine hydrochloride. The eyes were proptosed, and the epithelium was removed by rubbing with gauze swabs, as previously described.

Two per cent fluorescein sodium was used for staining. This acted as a guide to the extent and completeness of denudation. The sodium salt of penicillin was used in a concentration of 500 Oxford units per cubic centimeter of isotonic solution of sodium chloride. Four drops of this solution, pH 8, were applied hourly to the right eye of each rabbit. Application was started immediately after denudation had been completed. The treatment ran from 8 a.m. until 12 o'clock.

TABLE 3.—Influence of Local Applications of Penicillin on Regeneration of Corneal Epithelium

No. of control eyes healed on each day	Day of Regeneration					
	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth
2	1	2	3	1	3	
4	2	2	2	1	1	

midnight each day. Application of penicillin was also continued for twenty-four hours after each cornea failed to stain with fluorescein. The left eye of each rabbit acted as the control and received no therapy.

13 Adler, F. H., Leopold, I. H., and Steele, W. H. Unpublished data.

All the eyes were examined and stained daily. The results are recorded in table 3.

Comment.—It is evident from these data that local application of a solution of penicillin has no deleterious influence on the regeneration of corneal epithelium. Therefore it is safe, from this standpoint, to make repeated local instillations of the solution of penicillin in prevention and treatment of infection of the cornea.

CONCLUSIONS

1 Penicillin in solution or in ointment fails to penetrate into the aqueous humor of the normal rabbit eye after one local instillation but penetrates readily into the anterior chamber of rabbit eyes with corneal abrasion or with corneal ulcer.

2 The concentrations obtained in the anterior chamber of the eyes with inflamed or abraded

corneas after local instillation of penicillin exceed the probable therapeutic level.

3 It is not necessary to resort to iontophoresis, the corneal bath technic or subconjunctival injection in order to obtain effective concentrations of penicillin in the aqueous humor of eyes with infected corneal ulcers or corneal abrasions.

4 Instillation of a solution of penicillin (500 units per cubic centimeter of isotonic solution of sodium chloride) or penicillin ointment (500 units per gram) need be made only once every two hours to the conjunctival cul-de-sac to maintain high concentrations in the aqueous humor.

5 Repeated applications of penicillin solution (500 units per cubic centimeter of isotonic solution of sodium chloride) do not retard regeneration of corneal epithelium significantly.

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EPIDEMIC KERATOCONJUNCTIVITIS

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Scattered epidemics of acute conjunctivitis, characteristically complicated by punctate corneal lesions, have occurred in the United States during the past few years. Since the disease first reached epidemic proportions in the shipyards on the Pacific Coast, it came to be called "shipyard conjunctivitis," or "California conjunctivitis." That it may have been present in California before it became epidemic is suggested by the fact that in 1938 Hobson¹ found 16 cases of a similar disease in a veterans' hospital at San Fernando, Calif. Rieke² estimated that 600 cases occurred in one shipyard in Oregon in 1941, and de Roeth,³ at the same time, called the disease "epidemic keratoconjunctivitis" and drew attention to its association with superficial punctate keratitis. Hogan and Crawford⁴ summarized the disease in a report of 125 cases from the San Francisco Bay region. It is interesting to note that in the epidemics on the Pacific Coast corneal lesions failed to develop in many cases.

In 1889 Fuchs⁵ reported 38 cases of a disease he called "superficial punctate keratitis," which occurred in epidemic form in Vienna. The

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During the early part of this study convalescent serum was drawn and prepared under the supervision of Dr J E Perkins and Dr R F Korns, of the New York State Department of Health. The major portion of the convalescent plasma was prepared by the blood bank of the Presbyterian Hospital, under the supervision of Dr John Scudder. Dr Murray Sanders and Mrs Rose Alexander tested all specimens, donors and recipients for the presence of antibodies.

1 Hobson, L C Acute Epidemic Superficial Punctate Keratitis, Am J Ophth **21** 1153-1155 (Oct) 1938

2 Rieke, F E Epidemic Conjunctivitis of Presumed Virus Causation Report of Estimated 600 Cases in One Shipyard, J A M A **119** 942-943 (July 18) 1942

3 de Roeth, A F Epidemic Keratoconjunctivitis Superficial Punctate Keratitis, Northwest Med **41** 246-248 (July) 1942

4 Hogan, M J, and Crawford, J W Epidemic Keratoconjunctivitis with Review of Literature and Report of 125 Cases, Am J Ophth **25** 1059-1078 (Sept) 1942

5 Fuchs, M Keratitis Punctata Superficialis, Wien klin Wochenschr **2** 837-841 (Oct) 1889

keratitis was preceded by acute conjunctivitis, and the disease appears to have been similar to, if not identical with, the disease now under discussion. In his description Fuchs stated that the condition was a form of superficial keratitis related to herpes of the cornea but not associated with the formation of vesicles, and that the corneal changes had a predilection for the superficial layers and were concentrated in the central portions of the cornea. He also emphasized that the disease was frequently unilateral and that after recovery from the acute condition pain, photophobia and lacrimation were common. Adler,⁶ von Reuss⁷ and others described a similar disease occurring in other parts of Europe at about the same time.

The next reports came from Bombay, India, where in 1900 Herbert⁸ observed 26 cases of a similar disease. American physicians who visited India between 1900 and 1920 spoke of seeing a severe conjunctivitis associated with corneal opacities which was not trachoma. In 1920 Kirkpatrick⁹ made a short report on the disease, and Wright,¹⁰ and later Kirwan,¹¹ described extensive epidemics in Madras, India. The disease became widespread in India and China between 1920 and 1933 and occurred in India, China and Malaya from 1933 to 1936, in Germany from 1938 to 1940 and in Malaya, again, from 1935 to 1938. Hamilton,¹² in a survey of ocular disease in Tasmania, described numerous cases of a similar disease, and

6 Adler, H Ueber Keratitis subepithelialis centralis, Wien klin Wochenschr **2** 713, 1889

7 von Reuss, A Keratitis Maculosa, Wien klin Wochenschr **2** 665, 1889

8 Herbert, H Superficial Punctate Keratitis Associated with an Encapsulated Bacillus, Ophth Rev **20** 339-345, 1901

9 Kirkpatrick, H An Epidemic of Macular Keratitis, Brit J Ophth **4** 16-20 (Jan) 1920

10 Wright, R E Superficial Punctate Keratitis, Brit J Ophth **14** 257-291 (June) 1930

11 Kirwan, E O Epidemic Superficial Punctate Keratitis in Bengal, Proc All-India Ophth Soc **3** 1, 1935

12 Hamilton, J B Eye Diseases Found in Tasmania Eight Year Survey, M J Australia **1** 45-47 (Jan 10) 1942

Holmes¹³ in 1941, estimated that 10,000 cases occurred in Oahu, Hawaii. From all reports it is probable that the present epidemic in this country began in Malaya, and spread to Hawaii and then to the west coast of the United States

EPIDEMIOLOGIC CHARACTER OF CASES IN NEW YORK

Perkins, Korns and Westphal¹⁴ summarized the epidemiologic character of the outbreak of epidemic keratoconjunctivitis which occurred in Schenectady, N.Y., in 1942. Their reports were based on observations in several thousand cases. The acute conjunctivitis in their series was bilateral in 56 per cent of cases, and corneal opacities developed in 85.5 per cent, in 28.4 per cent of the latter the opacities were bilateral. In 92 per cent of cases corneal opacities developed between the seventh and the twenty-third day of the disease. In examination a simple spotlight was usually employed, and it is possible that a higher incidence of opacities might have been found if the corneal microscope had been used. Even without the slit lamp, however, the incidence was much higher than that in any of the series previously reported on. The highest incidence of infection occurred in the medical dispensary, a fact suggesting that the dispensary may have been a source of contamination. In this connection, Sanders, Gulliver, Forchheimer and Alexander,¹⁵ in a study of an outbreak of the disease in New York city, suggested that some of the patients in their series may have become infected while visiting a physician's office.

In my own experience, a number of patients have undoubtedly contracted the disease in clinics. In several instances it has been possible to trace the source of the infection beyond reasonable doubt and to determine accurately the period of incubation. In the cases in which a single exposure was known to have taken place, the period of incubation was usually from five to seven days.

Two cases were of particular interest. In the first, a physician was called one evening to remove a foreign body from the eye of a patient. Examination revealed a moderate amount of

¹³ Holmes, W. J. Epidemic Infectious Conjunctivitis, Hawaii M. J. 1: 11-12 (Nov.) 1941.

¹⁴ Perkins, J. E., Korns, R. F., and Westphal, R. S. Epidemiology of Epidemic Keratoconjunctivitis, Am. J. Pub. Health, to be published.

¹⁵ Sanders, M., Gulliver, F. D., Forchheimer, L. L., and Alexander, R. C. Epidemic Keratoconjunctivitis: Clinical and Experimental Study of Outbreak in New York City, Further Observations on Specific Relationship Between Virus and Disease J. A. M. A. 121: 250-255 (Jan. 23) 1943.

edema of the upper lid, with some chemosis and conjunctival infection. He was unable to find a foreign body, after careful search. Six days later a similar condition developed in the physician's eye, which became typical epidemic keratoconjunctivitis. Subsequent examination of his patient revealed the presence of many corneal opacities. The second case was that of an attending ophthalmologist at the Vanderbilt Clinic. He was presenting patients with conjunctivitis to a group of medical students. One patient had early epidemic keratoconjunctivitis, the diagnosis of which was obscure. Five days after the demonstration the ophthalmologist noted a foreign body sensation in his left eye. The symptoms gradually became more severe until there were considerable chemosis and edema of the upper lid. The disease then pursued the usual course, corneal opacities developing on the eighth day.

Two other incidents have been called to my attention. The first involved the use of the tonometer in the diagnosis of epidemic keratoconjunctivitis. As frequently occurs the early diagnosis was obscure, so the intraocular tension was taken in order to rule out the possibility of acute glaucoma. The tonometer was then used with 2 other patients with chronic glaucoma, in both of whom epidemic keratoconjunctivitis developed on the fifth and sixth days respectively following the examination. The second incident involved the use of trial contact lenses and was called to my attention by Dr. F. H. Adler, of Philadelphia. In 2 patients who were given trial fittings of contact lenses epidemic keratoconjunctivitis developed on the fourth and sixth days respectively after the fittings.

In an effort to determine sources of infection a large number of patients were questioned carefully. Most of them complained of a mild infection of the upper respiratory tract in association with the disease. In view of the common occurrence of such an infection, this association may of course be merely incidental but it is not unlikely that ocular infections do occur from nasal droplets. The following cases are examples in point.

Miss N was an operating room nurse in a large local hospital. She came in contact with few people. On her day off she went on a shopping tour and visited several large department stores. To her knowledge, she did not encounter any one with acute conjunctivitis. One week after her tour acute conjunctivitis developed in her left eye, which became typical epidemic keratoconjunctivitis.

Miss C P was a director of occupational therapy in a large hospital for chronic diseases, and her directing duties were such that she rarely came in contact with any one except the personnel of her department. She

made a train trip, and, although she did not knowingly come in contact with any persons with acute conjunctivitis, eight days later there developed an acute form of what proved subsequently to be epidemic keratoconjunctivitis.

These cases illustrate the possibility of infection either by fomites or droplets from persons who may or may not have the disease.

Throughout this study, the occurrence of foreign bodies and the sensation of a foreign body in the eyes of patients in whom the disease developed has been considered noteworthy. Some patients interpret the sensation of scratchiness as indicating that the onset was due to a foreign body although no foreign body is subsequently seen. In reviewing the cases in which foreign bodies did occur, it seemed more likely that the patient was infected with the disease when the foreign body was removed than that the foreign body had carried the infection. The following case is of particular interest in this connection.

Mr P., a hospital employee, reported to Vanderbilt Clinic with the complaint of something in his left eye. With the use of tetracaine anesthesia, a small foreign body was removed from the cornea. Sulfathiazole ointment was placed in the eye, and the eye was covered. The following morning the corneal abrasion had healed, and the eye appeared normal. Six days later the patient returned with acute conjunctivitis. A tentative diagnosis of epidemic keratoconjunctivitis was made and subsequently confirmed when typical corneal changes occurred.

Thus, although the cases of epidemic keratoconjunctivitis in which there had been no previous contact with either a physician's office or a clinic are much more numerous, clinics and dispensaries cannot escape incrimination as sources of transmission. It is obvious that ophthalmologists and physicians in general should give scrupulous attention to the cleanliness of their hands and instruments in treatment of this disease and should adopt the practice of using individual droppers for solutions, instead of dropper bottles. The virus isolated by Dr. Murray Sanders (see next section) survives in most of the common solutions used in ophthalmologic practice but deteriorates rapidly and loses considerable virulence when kept at room temperature for from three to six hours.

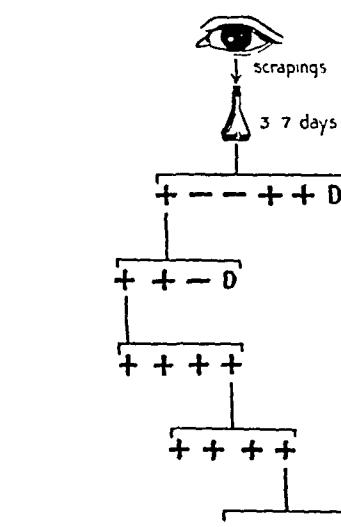
ETIOLOGIC FACTORS

In 1942 Sanders¹⁶ isolated a filtrable virus from scrapings of the conjunctiva of 2 patients with acute epidemic keratoconjunctivitis. He had inoculated a tissue culture with the conjunctival scrapings and had then injected the

tissue culture intracerebrally into mice. The following part of this study records an attempt to confirm Sanders' work.

Method of Study.—Scrapings from the conjunctivas of 25 patients with epidemic keratoconjunctivitis were suspended in fluid tissue cultures consisting of serum ultrafiltrate, balanced saline solution and brain tissue of the embryo mouse. In these cultures the mouse brain maintains viability but shows little evidence of growth. The inoculated cultures were allowed to stand at room temperature for periods varying from five to ten days. The tissue and fluid were then placed in the tissue culture grinder and carefully ground until no evidence of tissue remained. Six white Swiss mice (Rockland strain) were each inoculated with ground tissue culture, 0.05 cc being given intracerebrally and 0.15 cc intraperitoneally, and 0.5 cc was placed in a fresh tissue culture. The mice were examined daily for evidence of encephalitis.

Several of the 25 cultures were contaminated with pathogenic bacteria and were discarded. Inoculation of other cultures did not give rise to any symptoms in mice.



Unable to maintain potent virus

Fig 1.—Summary of results of attempts to isolate the virus from 25 patients. Here, — indicates a healthy mouse, +, a sick mouse, and D, that the mouse died. Sixteen mice recovered.

Apparent takes were obtained, however, with 10 cultures. The brains of sick mice were ground and 4 or 5 healthy mice inoculated in the emulsion. Attempts to step up the potency of the virus to a concentration at which it would consistently produce death in mice failed. Figure 1 illustrates the trend of the disease. Mice recovering from inoculation with the virus which were given intracerebral injections of Sanders' virus showed a high rate of recovery as compared with the rate for the control series (table 1).

Results.—There is little reason to doubt that I obtained a pathogenic agent from patients with epidemic keratoconjunctivitis. It produced transient symptoms of encephalitis in mice and could be transferred by serial passage from mouse to mouse, to tissue culture and back to mice. Its potency was not increased by serial passage. Since it produced a sublethal infection, it might reasonably be expected to produce immunity.

¹⁶ Sanders M. Epidemic Keratoconjunctivitis Isolation and Identification of a Filtrable Virus, *J Exper Med* 77:71-96 (Jan) 1943.

To test this hypothesis, 40 recovered mice were given to Dr. Sanders. He reported as follows: 'Forty mice which had survived intracerebral inoculation were given injections of stock epidemic keratoconjunctivitis virus in dilutions of 10^{-3} , 10^{-4} , 10^{-5} and 10^{-6} . A similar number of normal mice of the same age were given injections as controls. The results (table 2) were as follows: In 40 normal mice death occurred with all dilutions. In the test animals death occurred only with dilutions of 10^{-3} and 10^{-4} . No symptoms and no deaths were observed in the animals

the primary symptoms are those of sensation of a foreign body, with moderate itching and burning. The most striking features are edema of the upper lid, chemosis and edema of the semilunar fold and caruncle. The sensation of scratchiness present during this acute phase may be so intense and of such sudden onset that the patient is sure he has a foreign body. Edema is almost always striking, especially in the bulbar conjunctiva. In some patients the chemosis is so severe that the bulbar conjunctiva is exposed even when the eye is closed. The majority of

TABLE 1.—Results of Injection of Sanders' Virus in Animals Recovered from Inoculation with Virus from Conjunctival Scopings of Patients with Acute Epidemic Keratoconjunctivitis*

	Control Series				Recovered Series			
	10^{-1}	10^{-4}	10^{-5}	10^{-6}	10^{-3}	10^{-4}	10^{-5}	10^{-6}
1	—	—	—	—	—	—	—	—
2	D+++	+++D	++	—	—	—	—	—
3	DDD	DDD	++DD	++	++	D+—	—	—
4			DD	DD+	DD—	D—	—	—
5				DD	D—	—	—	—
6					—	—	—	—

* In this table, and in tables 2, 3 and 4, dashes indicate a healthy mouse, plus signs, a sick mouse, and D that the animal died.

TABLE 2.—Results of Intracerebral Inoculation of Epidemic Keratoconjunctivitis Virus into Forty Recovered Mice

	Date	Dilutions of Virus			
		10^{-3}	10^{-4}	10^{-5}	10^{-6}
First test	6/24	—	—	—	—
	6/25	—	—	—	—
	6/28	DDDD—	D D D—	—	—
	7/3	—	—	—	—
Second test	6/29	—	—	—	—
	6/30	—	—	—	—
	7/2	D—	—	—	—
	7/3	D D D D	—	—	—
	7/5	—	D D—	—	—
	7/6	—	D—	—	—
	7/13	—	—	—	—
Control	6/29	—	—	—	—
	6/30	—	—	—	—
	7/2	D D D—	—	—	—
	7/3	D D—	—	—	—
	7/5	—	D D D D	—	D D—
	7/6	—	—	D D D D	D D D—
	7/7	—	—	—	D D D D

which were given intracerebral injections of the virus in dilutions of 10^{-5} and 10^{-6} . This strongly suggests that the virus in your culture is similar to one isolated in this laboratory."

It seems, therefore, that the agent isolated in this laboratory may well be identical with the Sanders virus, my failure to obtain it in high concentrations accounting for the apparent differences between the two.

THE CLINICAL DISEASE

The signs and symptoms of epidemic keratoconjunctivitis are characteristic of hyperacute conjunctivitis. The disease may be divided into three stages. Stage 1 is an acute phase, in which

patients have moderate chemosis, associated with hyperemia of the conjunctival blood vessels. During this stage the eye frequently feels enlarged, and many patients have complained of pain and discomfort on rotation of the eyeball. This symptom may indicate changes in Tenon's capsule.

The disease enters the second stage in approximately forty-eight hours (fig 2). Large follicles and considerable subconjunctival infiltration develop, particularly in the lower lid, but in the upper retrotarsal fold and the fornices as well. The follicles in the conjunctiva are large, translucent and usually oval. Between follicles the conjunctiva shows moderate papillary hyper-

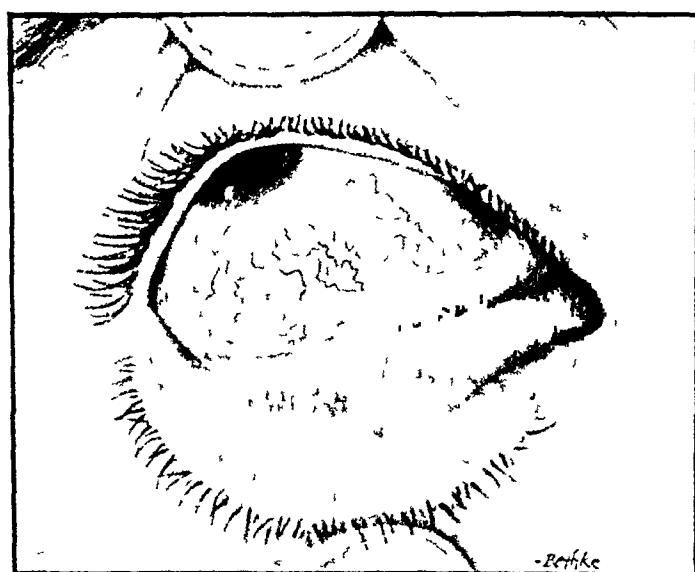


Fig 2—Appearance of the eye in the second stage of epidemic keratoconjunctivitis

trophy, with considerable hyperemia. During this phase there is nearly always a palpable, slightly tender preauricular lymph node. There may also be submental and submaxillary lymphadenopathy. It is during this phase that symptoms of involvement of the upper respiratory tract are often present, with a scratchy sensation in the throat. In some patients follicular pharyngitis has occurred. During both the acute and the follicular stages of the disease, tearing is a prominent symptom, and not infrequently the tears are blood stained. After from five to six days the edema decreases. The lymphadenopathy may be gone by the sixth day or may persist for several weeks. The tenderness of the lymph nodes rarely lasts beyond the sixth day. Frequently small hemorrhages are seen on both the bulbar and the palpebral conjunctiva but are not so severe as the hemorrhages accompanying acute pneumococcal conjunctivitis.

During this phase of the disease a pseudomembrane may develop on either the upper or the lower lid. It is thin as compared with the thick pseudomembrane of streptococcal conjunctivitis, but much thicker than the fine pseudomembrane associated with allergic conjunctivitis. In 67 per cent of this series a pseudomembrane was present by the third to the fifth day. Microscopic examination of the pseudomembrane shows it to be composed almost entirely of epithelial cells with mononuclear cells scattered throughout. Early in its development the slightly opaque translucent membrane is composed almost entirely of viable superficial conjunctival cells. Later, when the membrane is light yellow (usually on the fifth to the seventh day), it contains many more mononuclear cells and degenerating epithelial cells. I was unable to demonstrate virus inclusion bodies in any appreciable number, although the Giemsa method may reveal an occasional blue-stained body in the cytoplasm. The Victoria blue stain failed to demonstrate any free virus elementary bodies.

The third stage of the disease is characterized by persistence of the follicular conjunctivitis and the development of corneal changes. These changes produce symptoms of photophobia and blurring of vision. At times the blurring may be severe before any corneal opacities appear, owing to slight edema of the corneal stroma. Corneal opacities usually begin to form on the seventh or the eighth day (fig. 3). There is considerable variation in the manner in which they occur, but typically they begin as minute, discrete subepithelial dots. These dots increase in number to form opacities, approximately 1 mm. in diameter, located just beneath the epi-

thelium and seeming to lie in or on Bowman's membrane. They are usually circular and circumscribed by a sharp border. The epithelium over the surface is occasionally slightly raised but does not stain with 1 per cent fluorescein sodium. The opacities are concentrated in the central portion of the cornea and are usually most numerous over the pupillary area. Occasionally they are so numerous that they coalesce to form a gray opacity in the superficial layers of the cornea. In spite of their numbers and their proximity, it is almost always possible with the biomicroscope to see that they are composed of discrete nebulas and that they do not all lie in the same level of the cornea, some being on Bowman's membrane and some under it. When they are numerous photophobia is usually pronounced and there is considerable loss of vision.

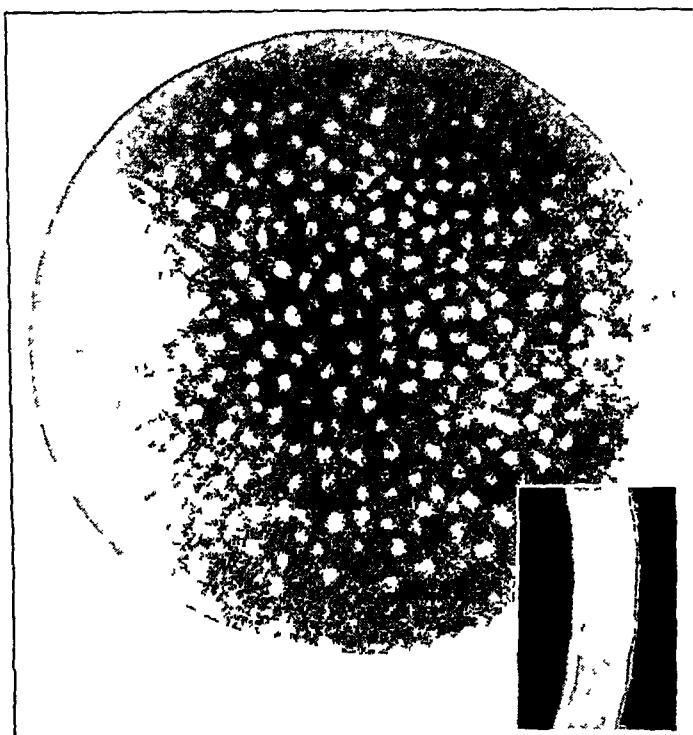


Fig. 3.—Appearance of corneal opacities in the course of epidemic keratoconjunctivitis.

The corneal opacities usually increase in number and size from the eighth to the twenty-first day, during which time the conjunctival signs are decreasing. The hyperemia gradually decreases, and the eye is white after three or four weeks. The blurring of vision and photophobia, especially in artificial light continue for several months, and many patients complained that if they did excessive near work there was a return of mild symptoms. Several patients were followed for periods up to eighteen months. The clearing of the opacities is a gradual process. The fine dots composing the opacities decrease in number, and the density gradually decreases, with increase in visual acuity. Vision is usually normal but "fuzzy" long before the opacities have

disappeared. Many of the opacities disappear without leaving any perceptible scar. In nearly all the patients followed for a long period one or two opacities remained visible with the slit lamp. In none of the patients did permanent loss of vision result. Bedell¹⁷ reported on the clinical observations in a large number of cases and also concluded that no permanent corneal damage results.

Pathologic Features—The pathologic elements were studied in conjunctival scrapings. No biopsies of the conjunctiva were made. The conjunctival epithelial cells appeared to be normal and showed no evidence of inclusion bodies, although, as previously mentioned, blue-staining bodies were noted in the cytoplasm of a few cells. Similar bodies have been observed with other types of conjunctivitis, and their significance is as yet unknown. In general the pathologic characteristics were the same as those already described by Hogan and Crawford.⁴ Large and small lymphocytes, with a few large mononuclear cells, predominated in the scrapings. Polymorphonuclear leukocytes were rarely seen, and only when there was bacterial contamination. From the character of the scrapings one would suspect that the follicle contributed many of the lymphocytes but that the entire conjunctiva was densely infiltrated with them. A striking observation in my cases was the unusual number of broken inflammatory cells. This may constitute a point of differentiation of the disease from Beal's conjunctivitis, in which lymphocytes also predominate but fragile cells are rare. The pathologic picture in mice has been discussed by Sanders.¹⁶ In this species the Sanders virus gives rise to mild lymphocytic encephalitis.

Bacteriologic Features—Early in the disease cultures were invariably sterile, while later, after considerable local medication, nonpathogenic staphylococci were almost always seen. Xerosis bacilli and other diphtheroids were recovered, and from a few patients *Staphylococcus aureus* was obtained. In the latter a few polymorphonuclear leukocytes sometimes appeared in the scrapings.

TREATMENT

The impossibility of making an unequivocal clinical diagnosis of epidemic keratoconjunctivitis before corneal opacities develop complicates the evaluation of methods of treatment, since rapid recovery and the prevention of corneal opacities constitute the criteria of effective treatment. Fortunately, however, Sanders¹⁶ provided a means of verifying the diagnosis when he showed that a patient recovering from the disease

possessed a substance in the blood serum which when mixed with dilutions of his virus prevented death in mice. This virus-neutralizing substance could be expressed by the reverse of the dilution factor. If the patient's serum-virus mixture diluted to titers of 10^{-1} , 10^{-2} , 10^{-3} , 10^{-4} , 10^{-5} and 10^{-6} killed mice in dilutions of 10^{-2} and 10^{-3} but failed to produce symptoms in higher dilutions, and if the normal serum-virus mixture diluted similarly killed all mice through dilutions up to and including 10^{-6} , the patient's serum had 10,000 units of neutralizing substance. Sanders¹⁶ observed that patients with other types of conjunctivitis, including Beal's, did not have this substance in their serum.

A total of 296 patients with epidemic keratoconjunctivitis were treated. Of these, 209 had symptomatic treatment. In all but 2 patients corneal opacities developed. In these 2 patients there was considerable doubt as to the accuracy of the original diagnosis, and, unfortunately, neither of them has been available for check-up of the antibody titer. Since the diagnosis for both patients was made during the height of the epidemic, however, their condition was classified as epidemic keratoconjunctivitis in spite of the questionable diagnosis.

Sulfonamide Compounds—Thirty-five patients were treated with sulfathiazole, 25 patients with an ointment containing 5 per cent sulfathiazole in anhydrous wool fat and petrolatum and 10 patients with 3 per cent solution of sodium sulfathiazole sesquihydrate. Clinically none of these patients was benefited by the therapy, and many of them complained that the local use of sulfathiazole ointment increased their symptoms. In an effort to evaluate therapy with the sulfonamide compounds experimentally, 48 white mice were fed sulfathiazole by mouth for two days and then given injections of various dilutions of the virus (table 3), 8 mice being used for each dilution. Five-tenths gram of sulfathiazole and 1.5 Gm of sodium bicarbonate were mixed with 100 Gm of a casein food, and each mouse received 5 Gm of the mixture a day. This is a standard method of protecting mice against streptococcal and pneumococcal infections. There was no evidence of protection against the virus, however, and treatment of 48 mice with sulfadiazine in a similar manner (table 4) yielded equally negative results. Clinically and experimentally sulfathiazole and sulfadiazine were observed to have no effect on the virus.

Penicillin—Local application of an ointment containing penicillin (500 units per gram of an oxycholesterol-petrolatum base) was used with 3 patients with no effect. Huang¹⁸ reported

¹⁷ Bedell, A. J. Epidemic Keratoconjunctivitis, New York State J. Med. to be published.

¹⁸ Huang Personal communication to the author.

to me that in his experience penicillin has had no effect on the virus when tested in vitro

Tyrothricin.—This drug was used for 10 patients in solutions of 48 and 20 mg per hundred cubic centimeters. Nearly all patients experienced some symptomatic improvement, but to about the same extent as that reported by patients using tetracaine and epinephrine. The duration of the acute phase of the disease seemed to be shortened, but in all 10 patients a large

factors are involved, however, since deaths in mice occurred erratically. One must conclude that experimentally tyrothricin had little or no effect on the virus and that clinically, although the severity of the acute conjunctivitis was decreased, the disease ran a normal course, this was true even though 2 of the patients were given tyrothricin on the first day of the disease.

Convalescent Plasma.—The presence of antibodies noted by Sanders suggested the ther-

TABLE 3.—Results of Feeding Sulfathiazole to Mice Inoculated with Virus of Epidemic Keratoconjunctivitis

Date	Dilution of Virus					
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶
5/17 Mice fed mixture *						
5/19 Injection						
5/20	----	----	----	----	----	----
5/22	D D D —	----	----	----	----	----
5/23	D D D D	D D D D	D D D D	D D D D	----	----
5/24				D	D D D —	D —
5/25					D —	----
5/26					D D —	----
5/27					D	----

* Each mouse data on which appear in this table and in table 4 was fed 5 Gm of a mixture containing 0.5 Gm of sulfathiazole sodium and 1.5 Gm of sodium bicarbonate per hundred grams of casein food.

TABLE 4.—Results of Feeding Sulfadiazine to Mice Inoculated with Virus of Epidemic Keratoconjunctivitis

Date	Dilution of Virus					
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶
5/17 Mice fed mixture						
5/19 Injection						
5/20	----	----	----	----	----	----
5/22	D D —	----	----	----	----	----
5/23	D D	D D D D	D D D D	D D D —	----	----
5/24	D D D D	D D D D	D D D D	D D D —	D D —	----
5/25			D D	D D D D	D D —	----
5/26					D D	----
5/27					D D —	D —

number of corneal opacities developed. Several in vitro tests were attempted. The results were difficult to evaluate, since the tyrothricin-virus mixtures when allowed to stand at room temperature did not kill mice in higher dilutions. After the mixture had stood two hours at room temperature few deaths occurred with dilutions of 10⁻⁵ and 10⁻⁶. A comparison of these results with those for the control series indicates that there is deterioration of the virus when it is allowed to stand at room temperature. Other

therapeutic use of convalescent serum or plasma.¹⁹ In order to test the effect of convalescent plasma on formation of antibodies, 5 patients with other types of conjunctivitis were given 50 cc and 1 patient was given 100 cc of the serum intravenously (table 5). Samples of blood taken from these patients at intervals up to three months were tested for the presence of antibodies.

19 Braley, A. E., and Sanders, M. Treatment of Epidemic Keratoconjunctivitis. Preliminary Report of Ten Cases, J. A. M. A. 121:999-1000 (March 27) 1943.

Only 1, the patient who had received 100 cc of plasma, presented any evidence of a neutralizing substance. She was a physician, with severe pneumococcal conjunctivitis involving her only eye, and she was given this amount of plasma.

TABLE 5—Results of Intravenous Administration of Plasma of Patients Convalescing from Epidemic Keratoconjunctivitis to Patients with Other Types of Conjunctivitis

Case	Diagnosis	Amount of Convalescent Plasma, Cc	Resultant Titer of Serum
1	Staphylococcal conjunctivitis	50	—
2	Pneumococcal conjunctivitis	100	10—(?)
3	Burns of skin	50	—
4	Acute conjunctivitis of unknown origin	50	—
5	Erythema multiforme	50	—
6	Chronic staphylococcal keratoconjunctivitis	50	—

TABLE 6—Results of Convalescent Plasma Therapy

Case	Name	No. of Days of Disease Before Administration of Convalescent Plasma	Amount of Convalescent Plasma, Cc	Results of Corneal Change	Final Titer of Patient's Serum
1	G T	8	50	1+	10,000
2	M T	3	40	—	10,000
3	B T	2	20	—	10,000
4	M N	5	40	—	10,000
5	A S	6	30	1+	10,000
6	J S	6	40	3+	10,000
7	D S	4	15	1+	1,000
8	J L	6	25	—	10,000
9	H T	5	50	—	1,000
10	M F	4	40	—	1,000
11	E L	5	50	—	1,000
12	W K	1	50	—	1,000
13	B M	2	50	—	1,000
14	L M	9	50	4+	10,000
15	H H	1	50	—	1,000
16	B S	3	50	—	1,000
17	W M	4	50	1+	1,000
18	E Y	1	50	—	1,000
19	H S	7 and 9	100	4+	100
20	A H	4	50	—	1,000
21	M G	2	50	—	1,000
22	M P	2	50	—	10,000
23	M L	3	50	—	1,000
24	L P	9	50	4+	10,000
25	J F	5	50	—	1,000
26	M G	4	50	—	100
27	W G	2	50	—	1,000
28	H C	3	50	—	100
29	S S	5	50	3+	1,000
30	H B	5	50	1+	1,000
31	W S	7 and 9	100	4+	10,000
32	L N	4	50	—	1,000
33	W L	3	50	—	1,000
34	W F	9	50	4+	100
35	W T	3	50	—	1,000
36	P P	2	50	—	1,000
37	T G	3	50	—	100
38	S S	4	50	—	1,000
39	L S	5	50	—	1,000
40	D D	4	50	—	100
41	B B	3	50	—	100
42	P H	2	15	—	100
43	F H	2	20	—	1,000
44	K M	3	30	—	100
45	M K	4	20	—	100
46	P G	3	15	—	100
47	G W	6	20	1+	100

because she had not responded rapidly to local sulfonamide therapy. She has not been available for a final check on the antibody titer of her serum, but it was very low at the end of two months. The conclusion drawn from these tests was that convalescent plasma given in amounts

of 50 cc was insufficient to affect the test for antibodies.

Convalescent plasma was administered to 47 patients for whom a diagnosis of epidemic keratoconjunctivitis had been made. Samples of serum were obtained from these patients at intervals (table 6). None of the serum which was obtained during the acute disease had virus-neutralizing antibodies. The neutralizing substances became apparent in from one to three months. Patient 19 is of particular interest because she did not show any response to the plasma, and the development of antibodies was slow. In spite of the presence of many corneal opacities, there was no evidence of antibodies until three months after the opacities developed.

When the results of this experiment are expressed in a graph, it is evident that little, or no, effect was obtained when the plasma was given after the seventh or eighth day (fig. 4), good

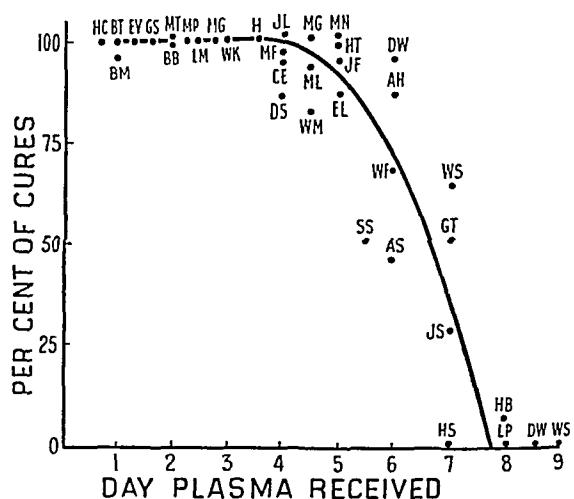


Fig. 4—Results of administration of convalescent plasma to 36 patients with epidemic keratoconjunctivitis.

results were obtained when the plasma was given before the fifth day, and inconsistent results, some good and some poor, when the plasma was given after the fifth day. Whereas corneal opacities developed in 99 per cent of all patients not treated with convalescent plasma, they developed in only 30 per cent of patients treated with convalescent plasma. Corneal opacities developed in the majority of patients treated after the fifth day. This failure of the convalescent plasma to effect cure after the disease was established is consistent with results obtained in the treatment of other virus diseases for which convalescent plasma or serum has been of value during the incubation period or the first days of the illness.²⁰

20 Van Rooyen, C E, and Rhodes, A J. *Virus Diseases of Man*, New York, Oxford University Press, 1940.

A control series of 5 patients with epidemic keratoconjunctivitis were given 50 cc of normal plasma intravenously (table 7) The normal plasma had no effect on the progress of the disease or on the development of antibodies in the serum

TABLE 7.—*Results of Injection of Normal Plasma on Patients with Epidemic Keratoconjunctivitis*

Case	Day of Disease Injection Was Given	Amount of Normal Plasma, Cc	Resultant Corneal Changes	Final Serum Titer
1	4	50	4—	1,000
2	6	50	4—	10,000
3	3	50	4—	1,000
4	5	50	4—	1,000
5	2	50	4—	100

COMMENT

Epidemic keratoconjunctivitis, while new to this continent, has occurred in epidemics elsewhere in the world In these epidemics observers have emphasized the presence of corneal opacities As in trachoma, in which pannus must be present before the diagnosis can be made, the subepithelial infiltration of the cornea characteristic of epidemic keratoconjunctivitis must be present before an unequivocal clinical diagnosis is possible The diagnosis can also be made on the basis of the development of virus antibodies, but as antibody titer can be detected only long after the disease has run its course, this method is of no value in making an early diagnosis In the acute phase of the disease, then, the diagnosis is presumptive and must remain so until corneal opacities develop or virus-neutralizing substances can be measured

SUMMARY AND CONCLUSIONS

Epidemics of a disease similar to epidemic keratoconjunctivitis have been reported at intervals since 1889

The current epidemic probably began in Malaya, in 1938, from whence it spread to Hawaii and to the continental United States

The epidemiology is obscure, but clinics, dispensaries and physicians' offices must be considered sources of transmission Scrupulous care should be given to the cleansing of hands and instruments, and the use of individual droppers is recommended

The clinical disease may be divided into three stages (*a*) abrupt onset of edema, associated with a foreign body sensation, (*b*) follicular conjunctivitis and pseudomembrane formation, with lymphadenopathy and symptoms of involvement of the upper respiratory tract, and (*c*) retrogression of the conjunctivitis with development of corneal opacities

The etiologic agent is probably a filtrable virus, the observations in the present study substantiating those of Sanders

Patients recovering from the disease have immune bodies for the virus in their serums

The sulfonamide compounds and penicillin have no effect on the virus

Tyrothricin probably has no effect on the virus

Convalescent plasma or serum, administered before the fifth day of the disease, is the treatment of choice

Corneal opacities developed in 99 per cent of the patients treated symptomatically but in only 30 per cent of patients treated with convalescent plasma

BRUCELLOSIS

LIEUTENANT COMMANDER HAROLD J HARRIS (MC), U S N R

Brucellosis is an infectious disease of manifold symptoms. The eye is one of the many sites of its manifestations, although the disease is relatively rarely recognized through its ocular signs. In its acute or its chronic form, brucellosis is second to no other disease, syphilis not excluded, in its ability to masquerade under innumerable guises.

Of the pathology, only enough will be said to show why the symptoms may be so varied. The organism has been isolated from the heart in cases of endocarditis and pericarditis, from the lung in cases of pleurisy and pneumonia, from the liver in cases of necrosis and abscess, from the gastrointestinal tract in cases of ulceration of the small and large bowel and of appendical infection, from the mesenteric lymph nodes, from the spleen in cases of necrosis, from the fallopian tubes in cases of salpingitis, from the ovary in cases of infected cyst, from the gallbladder in cases of acute and chronic cholecystitis, from the pancreas in cases of abscess, from the kidney in cases of pyelonephritis, from the bone in cases of osteomyelitis, from abscess of the mediastinum, from the joints in cases of acute and chronic suppurative and nonsuppurative arthritis and hydrarthrosis, from the testes, epididymis and prostate, from the skin in cases of chronic subcutaneous abscess and ulceration, from the mammary gland in cases of mastitis, from the tonsils, from the lymph nodes in virtually all regions of the body, from the central nervous system in cases of meningitis, encephalitis and myelitis, from the placenta, and from the human fetus. From all these tissues, as well as from the blood, spinal fluid, urine and stool, the organism has been cultured by one or more investigators.

There is no characteristic histopathologic picture. Proliferation of the cells of the reticuloendothelial system and infectious granuloma resembling the tubercle were pointed out by Sharp.¹ Confusion with tuberculosis was warned against by Amoss, by Fleischner and Meyer and by others.

Read at a meeting of the New York Society for Clinical Ophthalmology, May 1, 1944.

1 Sharp, W B Pathology of Undulant Fever, Arch Path 18 72-108 (July) 1934

OCULAR MANIFESTATIONS

Green,² of St Louis, published one of the earliest reports concerned exclusively with ocular manifestations in brucellosis. He stated that the occurrence of such signs in the course of brucellosis was well established but that comparatively few ophthalmologists had taken advantage of the opportunity to determine by laboratory methods the presence or absence of past or present infection with brucella organisms. He reported 4 of his own cases and cited 28 others from the literature, in 11 of which culture of the blood or the spinal fluid yielded the organisms. Green's own series included 1 case of recurrent phlyctenular conjunctivitis and corneal ulcer, 1 of retinal hemorrhage, 1 of optic neuritis and 1 of retinochoroiditis, clinically attributable to brucellosis. The cases reviewed included 1 or more each of the following conditions: iritis, optic neuritis (with or without atrophy), panophthalmitis, iridochoroiditis, septic retinitis, papilledema, hemorrhagic retinitis, palsies of ocular muscles, iridocyclitis, and keratitis, associated with or independent of brucella meningitis or meningoencephalitis.

Green pointed out that most ocular lesions occurring in the course of brucellosis do not destroy the integrity of the globe and that enucleation is therefore not demanded. This explains the lack of studies on the pathologic changes in the human eye. He called attention to Orloff's study of eyes of guinea pigs which had died. Orloff had stressed the practical importance of the ocular infections associated with brucellosis, commenting that they seemed to have great similarity, clinically as well as pathologically, to ocular tuberculosis.

Rutherford³ stated

Meliensis infection of the central nervous system occurs occasionally with or without ocular complications. [In 3 of 63 cases of undulant fever] there were bilateral papilledema, an increase in the spinal fluid pressure, mononuclear pleocytosis and evidence on which to base a diagnosis of infection of the central

2 Green, J Ocular Manifestations in Brucellosis, Arch Ophth 21 51-65 (Jan) 1939

3 Rutherford, C W Papilledema in Undulant Fever Report of Cases, J A M A 104 1490-1492 (April 27) 1935

nervous system by some variety of the melitensis organism

Papilledema is occasionally found in patients in whom the symptomatology is indefinite and leading signs are absent. It is in such cases that undulant fever should be considered in the differential diagnosis.

Carpenter and Boak⁴ also noted the lesions of the eye produced by brucella infection and stated that they were similar to those produced by infection with the tubercle bacillus. That many cases of Brucella involvement of the eye have been ascribed to tuberculosis can scarcely be doubted.

Braley⁵ saw several cases of choroiditis associated with chronic brucellosis but was never able to isolate the organism. He noted that the eyes healed rapidly with vaccine therapy and that they also healed with no treatment but healing required more time. In various cases he ascribed acute iritis, acute choroiditis and chronic iritis, iridocyclitis and choroiditis to brucellosis.

There seems good reason to bear in mind Green's comment²

An immense amount of work has been done on brucellosis in the past twenty years. Those who have undertaken the study of the disease either in the laboratory or clinically have become enthusiastic about the possibilities and implications of this new malady, in fact, one is inclined to feel that some authors have allowed their enthusiasm to outrun their judgment. Evidence is accumulating, however, that some ocular maladies ascribed to other origins may be caused by brucellosis. The external ocular muscles, the cornea, the uveal tract, the retina and the optic nerve have all proved vulnerable. Who has not been thwarted in his most painstaking efforts to establish the cause of a chronic uveitis? Should not the ophthalmologist include in his list of possible etiologic factors a disease that is widespread and one which has been proved to be capable of affecting almost every tissue of the body?

Although I have been thought to be one of those who are overenthusiastic about the possibilities and implications of this infection, I have reported few instances of ocular involvement.⁶ This was due not to the paucity of cases with ocular manifestations but to my almost complete lack of knowledge concerning the eye, which prevented evaluation of the cases encountered. The ophthalmologists to whom these patients were referred treated them empirically, also without suspecting the origin of their infection. Fortunately, there were few serious eventualities, either because there was

⁴ Carpenter, C. M., and Boak, R. A. Undulant Fever. Sources, Modes of Infection and Prophylaxis, Am J M Sc 185: 97-109, 1933.

⁵ Braley, A. Personal communication to the author, April 1944.

⁶ Harris, H. J. Brucellosis (Undulant Fever) Clinical and Subclinical, New York, Paul B. Hoeber, Inc., 1941.

spontaneous remission or because these patients also were treated with brucella vaccine.

The greatest handicap in the proper evaluation of ocular involvement—or indeed in any manifestation of brucellosis—is the difficulty in obtaining accurate cultural studies. This is due not only to the lack of interest on the part of most bacteriologists, and laboratory technicians, and, I am sorry to say, of physicians also, in this so-called rare disease, but to the technical difficulties in growing the organism, especially the Brucella abortus strain.⁷

One of the first patients in whom I noted ocular manifestations was a school teacher aged 35 who was referred to me by Dr. Ralph Greene.⁸ She had had repeated exacerbations of brucellosis for several years, with diplopia and a recurrent cervicosympathetic syndrome with each attack.

Probably my first recognition of iritis⁹ as a part of the clinical manifestation of brucellosis occurred in May 1941, not long after the beginning of my Naval service.

A sailor aged 24 was sent to me for an opinion as to whether he was malingering, psychoneurotic or really sick. He complained of headache, joint and muscle pains, epigastric distress, pronounced fatigue and productive cough. No cause for his complaints had been found during three months of careful study except for moderate secondary anemia and recurrent severe iritis. The results of all studies were without significance until the tests for brucellosis were made. The iritis had recurred four or five times a year, together with low grade fever, over a period of five years. Each summer for eight years there had been attacks of chills and fever of unknown origin, the period of the attacks lasting from three to five weeks. An agglutination test of the blood for brucellosis gave a negative reaction (as is usually true with chronic brucellosis), the cutaneous reaction was positive, and the phagocytic index was low. The patient was transferred to my wards for further observation. Br. abortus vaccine was given, with only temporary improvement in the subjective symptoms and in the recurrent attacks of iritis. The iritis at first recurred in spite of vaccine therapy, until use of the vaccine intravenously was followed by a high phagocytic response and freedom from the attacks for several months. I was detached from the hospital shortly after the attack on Pearl Harbor and so was prevented from ordering a trial of artificial fever therapy for him. About a month later, because of his failure to recover completely from his illness, which had existed long before his enlistment, he was discharged from the service. Three months after I had last seen him his family reported that he had had another attack of iritis, that there had

⁷ Poston, M. A. Studies in Chronic Brucellosis III. Methods Used in Obtaining Cultures, Pub Health Rep 53: 1-4, 1938.

⁸ Greene, R. Personal communication to the author, May 1941.

⁹ Harris, H. J. Chronic Brucellosis with Recurrent Iritis, Hemiplegia and Death from a Complicating Diffuse Encephalitic Encephalomalacia, U. S. Nav M Bull 41: 517-520, 1943.

been several attacks of vertigo, during one of which vision was much reduced and that twice he had stumbled and fallen, for no apparent reason, while going upstairs. For ten days he had complained of severe headaches, usually lasting only a few minutes and generally accompanied by stiffness of the neck. Soon thereafter sharp pain had developed in the left frontal region, and about four days later his right leg became weak, with a tendency to limp. He had noted difficulty in concentrating. On March 20, 1942 he had sudden right hemiplegia and was admitted to the University of Kansas Hospital, to the service of Dr Frank Teachenor. His right pupil was slightly larger than the left, both pupils reacted to light, and there was a questionable degree of choking of the left optic disk. The spinal fluid examined on April 3, 1942, was under 260 mm of pressure and was clear, with 33 white cells (85 per cent lymphocytes) per cubic millimeter and 119 mg of total protein per hundred cubic centimeters. On April 9 a ventricular cannula passed toward the left lateral ventricle through a burr hole just to the left of the midline met with lack of the usual resistance. A biopsy cannula, passed into the same region of the frontal lobe, brought forth soft, reddish brown, granular tissue. Operation was discontinued, but the patient died the same day. Histologic examination, by Dr H R Wahl, showed extensive acute and chronic inflammatory reaction in the pons and in the region of the left internal capsule, with a well marked, cufflike accumulation of monocytes and polymorphonuclear leukocytes in the perivascular spaces. Dr Wahl stated that death was due to "a rather severe acute and chronic form of encephalitis," which conformed to the type reported by Sharp,¹ De Jong¹⁰ and others as of brucella origin.

Dr William Rose referred a woman aged 26 to me on June 13, 1942 for performance of the multiple tests for brucellosis because of the suspicion that her attacks of keratitis and conjunctivitis might be due to this condition. The attacks had been recurrent for about four years and were confined to the right eye. They were accompanied with severe pain, headaches, tearing and progressive loss of vision, clearing up for varying periods except for residual blurred vision. Use of the eyes seemed to precipitate attacks. Herpetic keratitis, vitamin deficiency, allergy, anemia and syphilis had been suggested and ruled out as etiologic factors. In addition to the ocular manifestations, the patient had complained of weakness, mental confusion, joint and muscle pains, headache and vague gastrointestinal symptoms. She was afebrile, but there was a history of recurrent chills and fever three or four years previously. She had drunk raw milk for many years. On June 13 the agglutination reaction was negative for brucellosis, the cutaneous reaction positive and the phagocytic index low (phagocytosis was pronounced in 2 cells, moderate in 8 cells, slight in 12 cells and absent in 3 cells, index, 2-8-12-3). The presence of the positive cutaneous reaction was interpreted as evidence of a past or still existing brucella infection. The low phagocytic index in the presence of the positive cutaneous reaction and systemic symptoms referable to brucellosis was interpreted as presumptive evidence of brucellosis from which the patient had not recovered. Br abortus vaccine was administered as a therapeutic test by Dr Rose, and there was steady improvement both in constitutional manifestations and in the ocular condition coincident with a pronounced rise in the phagocytic index.

On July 27 the opsonocytophagic index was 16-9-0-0 and on August 22 it was 20-5-0-0. On this date the patient reported that she felt entirely well and showed great improvement in the condition of the eyes. Within four months there was complete clinical recovery, and the phagocytic index still showed a high degree of resistance (18-7-0-0). There has not been any recurrence of keratitis for more than eighteen months, and the patient has been working steadily for over a year. There was a recent mild recurrence of constitutional symptoms, accompanied, as is so frequently significant, by a fall in the phagocytic index to 5-7-6-7. Soon after vaccine treatment was again instituted, these symptoms disappeared coincidentally with a satisfactory rise in the phagocytic power of the white cells. There were no ocular manifestations.

Brucella vaccine treatment cannot be relegated to the category of nonspecific shock therapy. In the majority of patients reactions to vaccine are best avoided entirely. The clinical improvement almost invariably parallels the rise in the phagocytic power of the white cells, and relapse all too often occurs if the phagocytic index is not kept at a high level until there has been a long period of clinical recovery. The response that has so often been reported to follow intravenous administration of typhoid vaccine may be the result of nonspecific shock therapy, or it may produce whatever doubtful results are obtained through production of fever. No one has shown that such nonspecific therapy produces more than transient improvement. In patients treated with this method early in my work¹¹ with brucellosis, in 1932 and 1933, relapse occurred so soon and so consistently that the method was abandoned. The good results reported by many authors were, I believe, published too early and represented too small a number of cases to be considered significant.

Two brothers were recently referred to me for an opinion by Dr A C Krause, chief of the department of ophthalmology of the University of Chicago. One of them, aged 37, had a history of recurrent uveitis since April 1943, preceded by a history of chronic arthritis since 1937. The other patient, aged 44, had a history of iritis, keratitis, conjunctivitis and episcleritis, involving first the right and later the left eye, which had been recurrent since 1938. In 1940 his tuberculin reaction had been moderately positive, and the intradermal test with brucella antigen had given strongly positive results. The agglutination reaction had been negative for brucellosis. Ten days after the cutaneous test for brucellosis a small paracentral scotoma on the right of the fixation point was noted in the left eye. Two weeks later, thirty-six hours after injection of 0.1 cc of a mixed filtrate of brucellas, a central scotoma appeared, and a small reddened area of hemorrhage was noted just above the fovea. The diagnosis was acute chorioretinitis, with macular edema, hemorrhage and absence of the macular reflex, in the left eye. A month later two globular hemor-

¹⁰ De Jong, R N. Central Nervous System Involvement in Undulant Fever with the Report of a Case and a Survey of the Literature, *J Nerv & Ment Dis* 83:430-442, 1936.

¹¹ Harris, H J. Undulant Fever (Brucellosis) Difficulties in Diagnosis and Treatment, New York State J Med 37:1295-1301, 1937.

rhages, nasal to the macula, were noted. In March 1942, after regression of this process, new small hemorrhages appeared nasal to the macular region of the left eye. Careful study for evidence of perivascular disease, including biopsy of muscle tissue, gave negative results. Further hemorrhages were noted in April, June and July 1942. In October 1942 the patient exhibited a central scotoma 10 degrees in diameter in the left eye. At that time he complained of severe fatigue. A diagnosis of chronic brucellosis and central retinitis, probably due to brucellosis, was made by Dr. Krause. Other laboratory studies showed a relatively low white blood cell count, ranging from 3,800 to 5,900, with a normal differential count. In March 1942 the sedimentation rate was 20 mm in one hour. Agglutination tests with *Br. abortus* prior to the cutaneous test gave negative results. The Wassermann and Kahn reactions of the blood were normal. Urine and all other routine and special studies revealed nothing abnormal.

The patient furnished additional data concerning himself, including the history of low grade fever and extreme fatigue (to the degree that he spent the winter of 1940-1941 in bed), arthritic pains and recurrent diarrhea, occurring between visits to the ophthalmic clinic. Bizarre results of urinalysis were reported. On Sept 17, 1943 there were a 2 plus reaction for albumin and a 3 plus reaction for sugar, hyaline casts and 2 to 3 pus cells per high power field. On December 28 there was no albumin and no casts, and the reaction for sugar was 2 plus. On Jan 26, 1944 examination showed a faint trace of albumin, no sugar and occasional hyaline and granular casts, with similar results on February 16. On May 14, 1943 the laboratory of the Illinois state department of public health had reported isolation of brucella organisms from a specimen of stool.

This patient's experience with a commercial mixed vaccine and with a mixed filtrate emphasizes one of the few dangers from vaccine therapy. Both the preparations may be productive of severe local, focal and systemic manifestations. With ophthalmic complications, as well as infections of the central nervous system, reactions are to be assiduously avoided. This can be accomplished by use of the plain *Br. abortus* vaccine, diluted to any necessary degree.

Abnormal constituents of the urine, such as are described in this case, are not rare in cases of brucellosis. Nephritis, as evidenced by albuminuria and the presence of hyaline and granular casts, has been encountered repeatedly in the course of brucellosis. To the coincident or unrelated appearance of glycosuria, with or without hyperglycemia, I⁶ have previously called attention.

DIAGNOSIS

In order to obtain an accurate diagnosis one must (1) disabuse one's mind of the almost universally prevalent idea that the agglutination test is the one and infallible diagnostic procedure and (2) evaluate properly the multiple tests that are available.

The agglutination test of the blood is negative in the majority of cases of chronic infection with

the brucella.¹² The positive reaction then is frequently in low dilutions only. This test, therefore, is valuable alone only when it gives positive results in dilutions of 1:80 or higher. A positive reaction in low dilution is suggestive of brucella infection, but may rarely occur as a cross agglutination in the presence of infection with *Pasteurella tularensis*, *Eberthella typhosa* or *Bacillus proteus* X 19. A negative reaction to the agglutination test does not rule out brucellosis. If that one point were sufficiently understood, fewer brucella infections would remain undiagnosed.

The intradermal test also has its limitations and points about which there is still confusion. Perhaps it is simplest to say that in all respects this test is comparable to the tuberculin test. A positive reaction indicates only that at some time the patient has been infected. It gives no information as to the present status of the infection. It is only in the presence of a moderate or low degree of phagocytic power of the white cells, plus clinical symptoms referable to brucellosis, that the cutaneous test becomes a valuable aid in diagnosis.

It is essential that the test not be ignored if the reaction is only weakly positive. A weakly positive reaction has the same significance as a strongly positive one, except that it indicates a lesser degree of sensitivity to brucella protein. This is a valuable guide to the proper dilution of vaccine to be used if vaccine therapy is indicated.

The test is preferably made with 0.1 cc of a heat-killed vaccine prepared from the *abortus* strain only, in a concentration of 2,000,000,000 organisms per cubic centimeter. The mixed vaccines are likely to produce unnecessarily severe reactions. Brucellergin,¹³ a filtrate of the three strains, is apparently much less sensitive as an antigen.¹⁴ The reaction should be read at the end of four days. If the result is then negative or equivocal, it should be read again at the end of seven or eight days because of the possibility of delayed reaction.

Like the agglutination test, the cutaneous test may give a negative reaction even in the presence of a positive culture.¹² However, if a sensitive

¹² Evans, A. E., Robinson, F. H., and Baumgartner, L. Studies on Chronic Brucellosis IV. Evaluation of the Diagnostic Laboratory Tests, Pub. Health Rep. 53: 1507-1525, 1938. Harris⁶

¹³ Huddleson, I. F. Brucellosis in Man and Animals, New York, Commonwealth Fund, 1943.

¹⁴ Angle, F. E., Algie, W. H., Baumgartner, L., and Lunsford, W. F. Skin Testing for Brucellosis (Undulant Fever) in School Children, Ann. Int. Med. 52: 1189-1193, 1939.

antigen is used, such a result will occur in probably only about 5 per cent of cases.

The opsonocytophagic test is performed for two purposes (1) to determine the degree of specific resistance of the patient as an aid in interpreting the significance of the cutaneous reaction, and (2) to provide a base line for comparison with future tests if the patient is to have vaccine therapy. The test if performed alone has little significance.

The test must be done with the most careful technic. The specimen of blood must be fresh—not more than three hours old. A viable stock culture of the brucella must be regrown by transplantation on a fresh liver-agar or bactotryptose-agar slant and incubation for forty-eight hours before it is to be used for the test. Nonvirulent cultures will give falsely high readings. The blood film, made after the suspension of live brucella organisms has been mixed with the patient's blood and incubated, must be carefully prepared and well stained with Wright's or Hasting's stain. The actual number of bacteria ingested by each of twenty-five polymorphonuclear leukocytes must be counted. The number of cells showing pronounced, moderate, slight and no phagocytic activity gives the direct measure of the patient's resistance to brucella infection.

As already stated, patients under treatment with *Br. abortus* vaccine will show a progressive increase in the phagocytic power of the white cells which is virtually always commensurate with their clinical improvement. By means of regularly repeated determinations of the phagocytic index after cessation of treatment the patient's status may be accurately checked. Relapse may usually be predicted in the presence of a falling index in patients who are not actually free of infection.

The presence of the organisms on culture of blood, pus, urine, bile, prostatic fluid, stool, or other fluid or tissue furnishes the only definitive laboratory test. In cases of chronic infection culture is exceedingly unrewarding, especially infections with *Br. abortus*. Culture should be undertaken whenever possible, however, and with the most careful technic, 5 to 10 per cent of carbon dioxide in air and special mediums being used and prolonged observation made. Animal inoculation is essential to accurate results. The guinea pigs must be kept nearly sixteen weeks in some instances. Poston was able to recover the organism from the blood of 5 of 14 chronically ill patients for whom all tests, including culture by the usual methods, had given negative results. *Brucella melitensis* and *Brucella suis* are more readily recovered, particularly the *melitensis*

strain, in the presence of the febrile illness. The great need is for laboratories in which there are facilities for and personnel interested in these procedures. In addition to its furnishing positive proof of diagnosis, a positive culture may be of inestimable value in pointing to the localization of infection, and therefore to measures for its eradication.

TREATMENT

In cases of the acute illness the most valuable aid is sulfadiazine or sulfathiazole, although neither substance may be said to be actually curative. Remission is likely to occur, at which time vaccine may be employed for the purpose of building up adequate resistance. Transfusions of immune or nonimmune blood may be successful, as may Foshay's antiserum, in bringing about remission. To bring about actual cure is the problem. Artificial fever therapy is, I am afraid, overrated in some quarters, for either the acute or the chronic illness. It is successful probably in only a small percentage of cases.¹⁵ Much of the probable error in its evaluation has been made on the basis of too hasty a decision as to recovery and of inadequate follow-up study. However, its trial is justified in selected cases, especially those in which the disease is refractory to vaccine therapy.

In intestinal localization of infection, succinyl-sulfathiazole or sulfaguanidine may prove to be of greatest value, especially in prevention of relapse.

In treatment of the chronic illness vaccine made from the *abortus* strain alone has proved to be of greatest value in my experience. Satisfactory results in approximately 75 per cent of more than 400 patients treated by this method have been achieved, with good results in 15 or 20 per cent and failures in 5 to 10 per cent. When vaccine fails to bring about recovery through intramuscular use, it is usually tried intravenously. By this route rather sharp reactions are usually produced, whereas reactions are deliberately avoided with the intramuscular administration. Use of O'Neil and Foshay's¹⁶ nitrous acid-treated vaccine is also a valuable

¹⁵ Harris, H. J. Physical Therapy of Various Manifestations of Brucellosis (Undulant Fever), *Arch Phys Therapy* **21** 605-611, 1940; Brucellosis, *Bull New York Acad Med* **19** 631-655, 1943. Simpson, W. M. Brucellosis (Undulant Fever), in Tice, F. *Practice of Medicine*, Hagerstown, Md., W. F. Prior Company, Inc., 1940, vol 4, chap 24, pp 99-108. Harris⁶

¹⁶ O'Neil, A. E. Preliminary Note on the Treatment of Undulant Fever in Man with Detoxified Vaccine and with Antiserum, *Ohio State M J* **29** 438-439, 1933. Foshay, L. Personal communication to the author, September 1939.

method in management of the chronic or the subacute illness.

The sulfonamide compounds are usually of little value for the chronic illness except in cases of localized infections. Succinylsulfathiazole gives some promise when there are repeated recurrences in the presence of intestinal localization. In treatment of the acute or subacute brucella arthritides, azosulfamide and sulfathiazole have given splendid results.

It must be emphasized that there is no blanket method for treatment of all patients with brucellosis. Each patient presents an individual problem. Penicillin, or other mold derivatives, may ultimately prove to be the uniformly effective agent. To date, these preparations have given no promise of being effective in gram-negative bacillary infections, although early observations with penatin¹⁷ (a protein antibacterial substance present in the crude filtrate of *Penicillium notatum*) were somewhat encouraging.

To date, the only commercially available preparations of brucella vaccine have been those con-

taining the abortus and suis, or abortus and melitensis strains, or all three strains of the brucella. These may give undue reactions in cutaneous tests and in therapy. There is definite evidence that they have less effect in stimulating specific resistance than does the abortus strain alone, even in the presence of infections with Br. melitensis.¹⁸ Recently a manufacturer of biologic preparations arranged to market a heat-killed Br. abortus vaccine, to be prepared from the same strain, of human origin, as the vaccine now prepared by the division of laboratories and research of the New York state department of health. When used in proper dilutions this vaccine should go a long way toward solving the problem of treatment in most cases of chronic brucellosis. Another manufacturer of biologic preparations has prepared the abortus strain of vaccine alone for the past several years, on special order.

In conclusion, I should like to express disagreement with the popular concept "that brucellosis is a rare disease and that there is no known method of treatment, in any event."

17 Kochalaty, W. Personal communication to the author, March 1944.

18 Calder, R. M. Chronic Brucellosis, South M J 32 451-460, 1939.

SULFADIAZINE IN TREATMENT OF DACYROCYSTITIS OF THE NEWBORN

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The treatment of simple epiphora or epiphora complicated by dacryocystitis occurring soon after birth is based on the premise that an obstruction is present at some point along the nasolacrimal duct. The types of obstruction may well be considered as (1) anatomic and (2) accidental.

The anatomic obstructive agent has been observed to be (1) an incomplete or delayed perforation of a thin membrane separating the lower end of the duct from the inferior meatus or (2) a congenital narrowing of the duct or a stricture in the canaliculus or at the entrance or exit of the lacrimal sac or within the nasolacrimal duct. It is difficult to see how employment of anything short of mechanical means would be logical treatment in a case of dacryocystitis resulting from an anatomic obstruction. In a case of this type, therefore, failure to effect a cure by digital pressure supplemented in certain instances by irrigation of the sac and the use of simple antiseptics, has generally been considered an indication for probing. It is well known that digital expression of the sac and probing when indicated leads to cure of the infection and recovery of function in the vast majority of cases.

It is possible, however, that consideration of the disease on the basis of an accidental etiologic factor might lead to the employment of even more conservative, and newer, methods of treatment which involve little risk and offer a reasonable chance of success. Furthermore, if an anatomic obstruction were always the cause of the dacryocystitis, there obviously would be few instances of spontaneous recovery and few reports of effective treatment by medical methods, including chemotherapy.

The accidental causes of epiphora and dacryocystitis in the newborn are (1) accumulations of epithelial, mucoid or mucopurulent material forming plugs within the nasolacrimal duct or on the floor of the nose under the middle portion of the inferior turbinate or (2) inflammation and edema of the nasolacrimal duct secondary to nasal infection. A review of the literature and the results of medical treatment in the 2 cases here reported indicate that such causes as ac-

cumulations in the nasolacrimal duct or infection should be considered when treatment is undertaken. Larsson¹ called attention to the frequency of spontaneous cure, which emphasizes the possibility of accidental etiologic factors, and cited Comberg and Riser as asserting that a spontaneous rupture of the thin membrane blocking the lower end of the duct has been known to occur four months after birth. Judge² emphasized how frequently a collection of secretion and epithelial debris in the inferior meatus obstructs the nasolacrimal duct and is the cause of chronic dacryocystitis in the newborn. He urged the removal of this material by suction or cleansing as part of the initial treatment in all cases. He attributed the spontaneous recovery of dacryocystitis in the newborn to clearance of the inferior meatus by sneezing. Edwards³ expressed the belief that the obstructions seen in the newborn were frequently due to clumps of epithelial cells or mucoid plugs within the duct or in the region of the inferior turbinate and suggested that pressure exerted through the sac would remove the obstructing substance. Hardesty⁴ reported having carried out treatment in 60 cases of tearing in the very young during the preceding five years. In 34 per cent recovery was spontaneous, and in 66 per cent at least one probing was required. He made a plea for timely treatment, anticipating the probability of infection if simple epiphora was allowed to go on unchecked. He emphasized that drainage was seldom established after infection had occurred without at least repeated irrigations. It has been generally recognized, and the belief was expressed again in an article by Walker,⁵ that a stricture in the canaliculus gives rise to uncomplicated

1 Larsson, S. On Treatment of Congenital Atresia of Nasolacrimal Duct, *Acta ophthalmologica* **16** 271, 1938

2 Judge, H. V. Dacryocystitis of Newborn, *New York State J Med* **41** 25 (Jan 1) 1941

3 Edwards, D. L. Remarks on Treatment of Dacryocystitis, *J Oklahoma M A* **32** 199 (June) 1939

4 Hardesty, J. F. Obstruction of Lacrimal Passages in Newborn Infant, *J Missouri M A* **38** 40 (Feb) 1941

5 Walker, J. D. Stenosis of Nasolacrimal Duct, *Texas State J Med* **37** 544 (Dec) 1941

epiphora, whereas obstruction lower down in the nasolacrimal duct might promptly be followed by infection of the sac, with persistence of chronic dacryocystitis, unless the flow of tears were re-established Reeder⁶ stated the belief that in the congenital type of chronic dacryocystitis there was, as a rule, just a mucous or an epithelial plug in the nasolacrimal duct, and he urged irrigation of the duct with isotonic solution of sodium chloride Harman,⁷ in discussing the treatment of minor conditions of the eye, called attention to the fact that epithelial debris generally blocked the duct, and he seemed satisfied that medical measures usually cured the condition Morgan⁸ reported having seen 3 infants a few days old in whom there developed a tense swelling over the lacrimal sac which persisted a few days and spontaneously disappeared He advocated digital massage, syringing of the duct and, when necessary, probing These men are but some of the authors who have suggested that there are factors in the dacryocystitis of the newborn other than anatomic obstruction, the opinion has repeatedly been expressed that epithelial and mucous plugs either in the duct or on the floor of the nose should be recognized as frequent causes of congenital epiphora and dacryocystitis It is probable that the epithelial plug referred to is related to the canalization of the nasolacrimal cord, indeed, the plug itself probably represents a failure of the central epithelial cells to separate and become necrotic⁹ If the epithelial plug is formed during embryonic life, it is hardly to be considered as directly related to infection, and little absorption by chemotherapeutic drugs would be expected This leaves, however, a group of cases in which infection is the exciting agent from the start Whether the infection causes edema of the mucosa of the nasolacrimal duct, with impeded outflow of tears and dacryocystitis, or produces the same effect by fostering the formation of a mucoid plug should make no particular difference in the response of the dacryocystitis to chemotherapeutic drugs

The frequent relief of dacryocystitis in the newborn by digital massage or syringing should not make the case against infection as a primary cause any stronger, for it is easy to see that infection in the duct system may bring about a mucoid

plug which is removed by digital pressure or syringing and the infection takes care of itself The acceptance, therefore, of the thesis that infection may of itself cause the obstruction in the nasolacrimal duct or be the means whereby a mucopurulent plug may develop will tend to rationalize medical treatment for a condition which is generally regarded as surgical In any event, infection is responsible for the mucous, and later the mucopurulent, secretion which follows blocking of the tears from any cause; and the least that can be expected from a trial of chemotherapy is clearing up of the infection, and then the obstruction, if anatomic, can be dealt with by probing The success which followed the giving of sulfadiazine in the 2 cases reported here seems more than accidental and tends to modify one's understanding of the development of dacryocystitis in the newborn

REPORT OF CASES

CASE 1—L M S, a white girl aged 7 months, was seen for the first time on Feb 1, 1944 The mother stated that the baby's eyes were normal until late in December The right eye began to tear, and an abscess of the lacrimal sac developed rapidly, with spontaneous rupture within a week The edema over the sac and eyelids had considerably improved during the preceding month; but the discharge had not disappeared, and there was moderate brawness over the inner portion of the lower lid Examination on February 1 revealed three draining sinuses over the area of the right lacrimal sac, with considerable surrounding induration and redness A small quantity of pus could be expressed from the sinus openings, which evidently led into the lacrimal sac There were moisture and mucus at the inner canthus, but pus could not be expressed from either punctum Unfortunately, no smear was made or material taken for culture at that visit The mother was ordered to give the baby 0.5 Gm of sulfadiazine at once and 0.25 Gm every four hours for the next three days, except for one dose at night The mother stated that within forty-eight hours the sinuses had healed over and no pus could be expressed from them The baby was examined in seventy-two hours, already the redness and induration of the skin were decreased, and there was no epiphora It was evident that the chronic dacryocystitis was healing rapidly Administration of sulfadiazine was continued for another twenty-four hours No blood count was made, and the amount of the sulfonamide compound in the blood was not determined No other treatment was given except for cleansing of the skin, and a thin application of an ointment containing 5 per cent sulfathiazole, 25 per cent hydrous wool fat and 75 per cent petrolatum was made every few hours to the sinus openings until they healed The child has been examined a few times since her recovery, the last examination being on June 8, and she is perfectly well The important features of the case are the absence of epiphora and the almost complete absence of scarring or redness over the area of the sac No pus, mucus or moisture could be expressed from either punctum at the last visit

CASE 2—T M, a white boy aged 5 months, was seen March 7, 1944 The mother stated that the baby's eyes were entirely normal until he was 2 months of age

⁶ Reeder, J E, Jr Surgical Treatment of Chronic Dacryocystitis, *J Iowa M Soc* **32** 15 (Jan) 1942

⁷ Harman, N B Treatment of Minor Conditions in Eye, *Brit M J* **1** 861 (April 16) 1938

⁸ Morgan, O G Observations on Treatment of Epiphora, *Tr Ophth Soc U Kingdom* **58** (part 1) 163, 1938

⁹ Riser, R O Dacryostenosis in Children, *Am J Ophth* **18** 1116 (Dec) 1935

At that time the left eye began to tear, and the onset was followed by a mucous, and later a purulent, secretion. The tearing and secretion had persisted, and the mother had been advised to employ digital expression of the sac and to keep the conjunctival sac free from any accumulation of secretion. Examination on March 7 revealed chronic inflammation of the left lacrimal sac. Considerable mucus and pus could be expressed from the sac, and there was a good deal of moisture at the inner canthus. A smear and culture of the secretion showed a pure growth of *Staphylococcus aureus haemolyticus*. The mother was advised to continue emptying the lacrimal sac by massage twice a day and to keep the conjunctival sac clean with a solution of boric acid. In addition, 0.5 Gm of sulfadiazine was ordered to be given at once and 0.25 Gm every four hours, except for one dose at night. Two days later the baby seemed much improved. The mother stated that for the first time in two months there had been no secretion in the conjunctival sac, and none could be expressed from the lacrimal sac. At the end of four days the dacryocystitis was entirely cured, and administration of sulfadiazine was discontinued. The baby has been seen regularly up to the time this paper was prepared, and there has been no recurrence of the symptoms. The important feature is the complete absence of epiphora.

COMMENT

Numerous articles concerning the use of the sulfonamide compounds for ophthalmic conditions have appeared in the literature during the last seven years. References to the use of the drugs in treatment of disease of the lacrimal sac, however, have been more casual than the subject merits, and few cases have been reported in the American journals. Marshall¹⁰ was one of the first investigators to estimate the level of a sulfonamide compound in body fluids and in body cavities after oral administration of the drug, and he proved that the substance did appear in empyema fluid in the pleural cavity. The earliest clinical summary of the use of sulfonamide compounds for ocular conditions was made by Hageman,¹¹ who reported on employment of sulfanilamide in treatment of gonorrhoeal conjunctivitis. Larsson¹ outlined the treatment of congenital atresia of the nasolacrimal duct but did not mention the use of chemotherapeutic drugs. Arruga¹² confined his article to the surgical treatment of lacrimation and inferred that any means of treatment other than surgical was generally ineffective. Jones¹³ discussed the increasing help received from the sulfonamide

compounds in management of diseases of the eye but did not refer to their use with infection of the lacrimal sac. The earliest report on the use of sulfanilamide in cases of dacryocystitis was by Castelli,¹⁴ in 1939. Redslob and his associates¹⁵ commented favorably on treatment with sulfapyridine in 9 cases of pneumococcal dacryocystitis. Excellent summaries, in which it was made clear that the sulfonamide compounds were of considerable assistance in ophthalmology, were published later in 1939 and 1940,¹⁶ but in none of these articles did the authors mention their having had experience with the sulfonamide derivatives in cases of dacryocystitis. Edwards,³ presenting the treatment of dacryocystitis ventured the opinion that sulfanilamide should be used in treatment of acute dacryocystitis and would be expected to assist in aborting an acute attack. Adler and McDonald¹⁷ recommended the internal use of the sulfonamide compounds in cases of acute suppurative dacryocystitis; they also employed the crystals of sulfadiazine locally in the sinus tracts after rupture of an acutely inflamed sac through the skin. Guyton and Woods,¹⁸ in their last review from the Wilmer Institute, reported prompt healing of acute dacryocystitis due to the Koch-Weeks bacillus when sulfanilamide was used. Landegger¹⁹ had not employed sulfanilamide in any case of disease of the lacrimal sac when he summarized his clinical experience in 1941. Goar²⁰ mentioned having insufflated sulfathiazole powder into a lacrimal fistula before operation, with good results. In the article previously referred to by

¹⁴ Castelli, A. La para-aminofenilsulfamide nelle dacriocistiti, *Boll d'ocul* **18** 523 (July) 1939

¹⁵ Redslob, E., Marx, P., Dieffenbach, P., and Milaras, T. Essai de chimiothérapie des affections gonococciques et pneumococciques de l'appareil visuel, *Bull Soc d'opt de Paris* **51** 326 (April) 1939

¹⁶ Guyton, J. S. Use of Sulfanilamide Compounds in Ophthalmology, *Am J Ophth* **22** 833 (Aug) 1939. Pryor, W. R. Sulfanilamide Its Effect on Eye, Ear, Nose and Throat, *Kentucky M J* **37** 305 (July) 1939. Glover, L. P. Some Use of Sulfanilamide in Ophthalmology, *Am J Ophth* **22** 180 (Feb) 1939. Rutherford, C. W. Sulfanilamide and Neoprontosil Recent Advance in Ophthalmic Therapeutics, *J Indiana M A* **33** 241 (May) 1940. Woodruff, H. W. Sulfanilamide in Ophthalmology, *Illinois M J* **78** 418 (Nov) 1940. Sykes, C. S. Sulfanilamide in Ophthalmology, *Texas State J Med* **35** 780 (March) 1940.

¹⁷ Adler, F. H., and McDonald, P. R. Paper read before the College of Physicians of Philadelphia, 1941

¹⁸ Guyton, J. S., and Woods, A. C. Advances in Use of Sulfanilamide Compounds in Ophthalmology, *Am J Ophth* **24** 428 (April) 1941

¹⁹ Landegger, G. P. Sulfanilamide in Ophthalmology, *California & West Med* **55** 200 (Oct) 1941

²⁰ Goar, E. L. Evaluation of Recent Therapeutic Agents in Ophthalmology, *Tr Am Acad Ophth* **46** 19 (Sept-Oct) 1941

¹⁰ Marshall, E. K., Jr. Determination of Sulfanilamide in Blood and Urine, *J Biol Chem* **122** 263 (Dec) 1937

¹¹ Hageman, P. O. Clinical Experience in Use of Sulfanilamide at New Haven Hospital, *J Pediat* **11** 195 (Aug) 1937

¹² Arruga, H. Surgical Treatment of Lacrimation, *Arch Ophth* **19** 9 (Jan) 1938

¹³ Jones, C. C. Use of Sulfanilamide in Otolaryngology and Ophthalmology, *J Iowa M Soc* **29** 6 (Jan) 1939

Walker,²¹ in which he discussed the symptoms and treatment of stenosis of the lacrimal duct, he presented 2 cases of congenital dacryocystitis in which sulfapyridine was given. In the first case, that of a baby 5 months old with a pneumococcal infection of the sac, sulfapyridine was given, but the infection was not brought under complete control until a probe was passed. In the second case, that of a baby 3 weeks old with pneumococcal infection of both sacs, in spite of the use of sulfapyridine irrigation of the lacrimal duct and local application of silver nitrate, each sac required probing for reestablishment of proper function and clearing up of the infection. During 1942 Heath,²² Rutherford²³ Scott²⁴ and Bellows²⁵ reported their experiences with use of the sulfonamide compounds but evidently they had not employed any of the compounds in treatment of diseases of the lacrimal sac. Braley²⁶ in listing ocular conditions with their specific etiologic organism recommended the oral administration of sulfadiazine or sulfathiazole for dacryocystitis caused by *Staphylococcus aureus*, the pneumococcus, *Streptococcus haemolyticus* and Friedlander's bacillus. Kolmer,²⁷ in a general discussion of chemotherapeutic drugs, said "The sulfonamide compounds should be worthy of use in the treatment of dacryocystitis." Sorsby²⁸ reported the use of sulfapyridine in 2 cases of acute dacryocystitis in which incision was required. The organisms responsible were the Koch-Weeks bacillus and the pneumococcus respectively. Sorsby seems to have concluded that the sulfonamide therapy was helpful but that the abscess required drainage. In a review of the literature preceding the report of his cases, Sorsby did not mention any reference to the use of sulfonamide drugs in the treatment of dacryocystitis. Spaeth²⁹ suggested the direct injection into the sac of sulfathiazole or its sodium salt.

²¹ Heath, P. Some Uses of Chemotherapy in Ophthalmology, *J. Michigan M. Soc.* **41** 303 (April) 1942

²² Rutherford, C. W. Chemotherapy in Ophthalmology (Review of Recent Literature), *J. Indiana M. A.* **35** 697 (Dec.) 1942

²³ Scott, G. I., in Symposium on Chemotherapy in Ophthalmology, *Tr. Ophth. Soc. U. Kingdom* **62** 3, 1942

²⁴ Bellows, J. G. Chemotherapy in Ophthalmology, *Tr. Am. Acad. Ophth.* **47** 19 (Sept.-Oct.) 1942

²⁵ Braley, A. E. Sulfonamides in Treatment of Ocular Infections, *Ohio State M. J.* **38** 1101 (Dec.) 1942

²⁶ Kolmer, J. A. Chemotherapy in Relation to Ophthalmology and Otolaryngology with Special Reference to Sulfonamide Compounds, *Tr. Am. Acad. Ophth.* **47** 36 (Sept.-Oct.) 1942

²⁷ Sorsby, A., in Symposium on Chemotherapy in Ophthalmology, *Tr. Ophth. Soc. U. Kingdom* **62** 15, 1942

as a means of treatment of dacryocystitis. Leopold and Scheie²⁸ used a 5 per cent suspension of the microcrystalline form of sulfapyridine or sulfathiazole for treatment in 7 cases of dacryocystitis. In the first 5 cases the pneumococcal infection cleared rapidly after three daily injections of 2 cc each of a 5 per cent suspension of sulfathiazole. The cultures were then sterile, and subsequently the obstruction in the lacrimal duct system was taken care of by additional means. In the sixth case, one of purulent dacryocystitis caused by the pneumococcus and the influenza bacillus, two injections of a 5 per cent suspension of sulfapyridine killed the pneumococcus, but even additional injections of sulfapyridine, and later sulfathiazole and sulfadiazine, failed to remove the influenza organism. In the seventh case an infection caused by the hemolytic streptococcus responded rapidly to two injections of sulfamilamide after injections of sulfapyridine had failed. The authors conclude that local injections into the sac of the sulfonamide compounds may prove a satisfactory method of controlling purulent dacryocystitis, at least temporarily.

Thygeson,³⁰ in an excellent review of the literature, which included certain instructions given to all medical officers of the United States Army,³¹ stated that sulfadiazine appeared to be the best of the compounds for treatment of this condition. He advised the use of sulfadiazine in all cases of acute and chronic dacryocystitis due to beta hemolytic streptococci, and he reported a single case of his own in which the condition healed rapidly.

In most of the aforementioned articles experience with dacryocystitis in adults is cited, but the situation with congenital epiphora and dacryocystitis is not so different that such information is not of considerable importance. There seems to be no dissenting opinion as to the usefulness of the sulfonamide compounds in treatment of dacryocystitis, and as the best drug to be used, with its dosage and route of administration, becomes established, this type of treatment will be more commonplace. A certain restriction, as to the route of administration of the drug at least, is placed on the treatment by the

²⁸ Spaeth, E. B. Résumé of Sulfonamide Drugs in Ophthalmology, *Pennsylvania M. J.* **46** 566 (March) 1943

²⁹ Leopold, I. H., and Scheie, H. G. Studies with Microcrystalline Sulfathiazole, *Arch. Ophth.* **29** 811 (May) 1943

³⁰ Thygeson, P. Sulfonamide Compounds in Treatment of Ocular Infections, *Arch. Ophth.* **29** 1000 (June) 1943

³¹ Chemotherapy in Infectious Diseases and Other Infections, United States War Department Circular Letter 17, Washington, D. C., Government Printing Office, May 1942

age of the patient, so it is likely that direct injection of a sulfonamide drug in solution into the lacrimal apparatus in babies will have a rather limited application because the procedure is fairly formidable and is comparable to probing. Oral administration to babies, however, is simple because the drug can be given with the formula, even if this method failed, the satisfactory report of Leopold and Scheie²⁹ would compel one to try local injections. It has always been of scientific interest at least to determine the organism responsible for an infection of the sac. Such information is more important than ever now, so a direct smear should be made and material for culture taken at the initial visit. The information obtained will be of considerable value in treatment and prognosis. The most common organisms responsible for infection of the lacrimal sac are *Staph aureus haemolyticus*, the pneumococcus, the beta hemolytic streptococcus, Koch-Weeks bacillus and Friedlander's bacillus. This group of organisms can be rather readily identified on smear and by culture and require no special mediums for growth. These organisms are all notably inhibited by the sulfonamide drugs except for the Koch-Weeks bacillus, and even this bacillus will at times respond to chemotherapy.¹⁸ Experimental and clinical investigation has produced evidence that the pneumococcus and gonococcus are more sensitive to sulfathiazole, while sulfanilamide is more active against the streptococcus. It is possible that sulfadiazine and sulfamerazine (sulfamethyl diazine) are active to an equal degree against all the organisms mentioned.

COMMENT

A review of the causes of congenital epiphora and dacryocystitis has shown that there is a factor of infection in all cases. This factor may be primary, in which case the entire process is dependent on bacterial invasion of the mucous membrane of the nose and the nasolacrimal duct. On the other hand, the infection may be secondary, in which case the underlying anatomic obstructive agent favored the development of infection by insufficient drainage of the tears.

In this paper the emphasis is placed on the element of infection and its cure. When a case of congenital epiphora with dacryocystitis is seen for the first time, it is impossible to know whether an anatomic obstruction exists, and for that reason chemotherapy in conjunction with other conservative treatment is to be recommended in all cases. It is probable that such treatment, especially if instituted early, will result in surgical treatments being required in fewer cases. The success of the oral administration of the sulfonamide compounds or the local injection of their microcrystalline form in clearing up the infection has been demonstrated, a complete cure will be obtained in many cases, and in cases in which simple epiphora remains separate means can be taken to remedy that situation.

The additional conservative treatment suggested consists of such conventional means as cleansing of the inferior meatus by suction, irrigation of the nasolacrimal duct with isotonic solution of sodium chloride and digital pressure on the distended lacrimal sac, in an attempt to rupture a congenital membrane or stricture.

From a survey of the literature on the use of sulfonamide drugs in ophthalmology, it is evident that the use of sulfonamide compounds for dacryocystitis, especially of the congenital type has not received the attention it deserves. It is possible that too much emphasis has been placed on a physical obstruction as the underlying factor in most cases of congenital dacryocystitis, even the digital pressure has been employed with the idea not of draining a chronic mucopurulent cavity but of rupturing an obstruction within the nasolacrimal duct by hydrostatic pressure. With the discovery of the increasing field of usefulness of chemotherapy, it is important that the drugs be employed in every disease of the eye or adjacent structures which offers the slightest chance of improvement.

SUMMARY

In 2 cases of congenital dacryocystitis a satisfactory response was obtained with administration of sulfadiazine.

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Clinical Notes

ACCIDENTAL VACCINIA OF THE EYELID WITH DISCIFORM KERATITIS

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Accidental ocular vaccinia is rare. Since the days of Jenner few cases have been reported in the literature and few physicians have had the opportunity of seeing a case. Such an accidental infection is seen first by the general practitioner, the family physician. It is proper therefore that the present case be reported. The diagnosis is problematic, but the history of vaccination of a member of the family will aid in recognition of the true nature of the condition. In reality the clinical picture is pathognomonic.

REPORT OF A CASE

M.R., a girl aged 14, was referred to my service at the Jewish Hospital by her family physician with the diagnosis of hordeolum. Four days before the patient had gone to a picnic in the park. Two days later the left eye became red and the lid swollen. The family physician referred her to the hospital.

Examination revealed that the right eye was normal, with vision of 20/20. The eyelids of the left eye, both upper and lower, were notably swollen and inflamed. The conjunctiva was chemosed, photophobia was pronounced, the cornea was somewhat hazy and because of irritation could not well be examined. The preauricular glands were enlarged and somewhat painful to the touch. The patient offered the statement that vision in the left eye had been as good as that in the right eye prior to the infection.

On the margin of the left upper lid near the outer canthus was a large ulcerated area covered with a white film which looked like a pseudodiphtheritic membrane. A few eyelashes were missing. A smaller ulcer, covered likewise with a white membrane, was seen on the nasal side of the margin of the same lid. On the margin of the lower lid there were three small, circumscribed, flat ulcers covered by a thin yellowish membrane characteristic of vaccinal ulceration in that area. The conjunctiva, while chemosed, was not ulcerated. There was no purulent discharge. A smear and culture of material yielded *Staphylococcus aureus*. The clinical picture was puzzling, and I asked Dr. Erich Urbach, allergist, to examine the patient. In answer to his question whether any one in the family had been

vaccinated, the mother replied that a younger sister aged 6 years, had been vaccinated two weeks ago and had been sleeping with the patient. On the basis of this history and the clinical picture, we concluded that the case was one of accidental transfer of vaccinia to the lid.

The patient refused to go to the hospital and was permitted to return home, with instructions to carry out the following treatment: use of sodium sulfathiazole, 3 per cent, as an eye wash, instillation of atropine sulfate solution, 1 drop three times a day and application of boric acid ointment at night. She was of course warned not to sleep with any one.



Appearance of left eye on tenth day of treatment

She returned three days later, when the swelling of the lids was much reduced, but the corneal haze had developed into a typical picture of disciform keratitis. Vision was considerably reduced and photophobia more intense. After three months of treatment the ocular process became quiet, with only a disk-shaped opacity on the cornea—left to tell the story of the infection.

There is no specific treatment for this condition, the therapy is purely symptomatic. My patient was vaccinated at the age of 6 years but apparently, after eight years, had lost her immunity to smallpox, as evidenced by the accidental infection with vaccinia. It is possible that this accidental vaccinia has conferred a new period of immunity on the patient.

[†]Dr. Brav died Dec 2, 1944

Ophthalmologic Reviews

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OPTOCHIASMIC ARACHNOIDITIS

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DEFINITION AND HISTORICAL REVIEW

One runs into difficulties at once in attempting to define optochiasmic arachnoiditis. The concept of this disease is gradually undergoing change, it is not today what it was, say twelve years ago, and I do not doubt that it will still evolve considerably. Even at present every one is not in complete agreement with regard to this condition.

I believe one may best approach the subject by outlining the several lines of converging thought by which the notion of optochiasmic arachnoiditis was arrived at. The first of these starts with acromegaly, which Pierre Marie,¹ in 1886, showed was due to a tumor of the pituitary gland. Such a tumor, later identified as acidophilic adenoma, grows upward, presses on the chiasm and causes visual disturbances, with bitemporal field defects. A few years later Babinski² proved that a pituitary tumor could be linked with a different clinical picture, eventually known as the Babinski-Frohlich syndrome. A tumor producing such a condition, now known to be a chromophobic adenoma, could also produce bitemporal hemianopsia, and during the first quarter of this century neurologists and ophthalmologists came to accept the idea that bitemporal hemianopsia was due to a chiasmic lesion, and therefore to a pituitary tumor. With the improvement of neurosurgical technic, operations for intracranial tumor became more numerous, and it was realized that the optic chiasm could suffer damage not only from an intrasellar growth under it but, in some instances, from a suprasellar tumor located above and anterior to it. In 1929 Cushing and Eisenhardt³ brought to the attention the meningomas

inserted on the tuberculum sellae, and after the thirteenth International Congress of Ophthalmology, held in Amsterdam in September 1929, it was generally accepted that a chiasmic syndrome with bitemporal hemianopsia could be produced not only by sellar but by suprasellar tumors. The next step followed at once, when it was understood that such bitemporal field defects could also result from pseudotumors, in the form of circumscribed collections of fluid, probably of inflammatory origin, occurring in the anterior, or perichiasmic, cistern. At the Amsterdam congress both Holmes⁴ and Cushing⁵ reported cases of such lesions.

The second train of thought leading to the concept of optochiasmic arachnoiditis started with Quincke, when he described generalized serous meningitis. A few years later Schlesinger⁶ showed that in some cases circumscribed collections of fluid were observed. The first of such pseudotumors were seen in the spine, but shortly afterward localized pockets of serous meningitis were observed to form on the lateral surface of the hemispheres. It was already suspected that the underlying nerve tissue was not normal and was also affected by an inflammatory process. In the early twenties, when the cerebellopontile angle was more readily explored, operation was performed in several cases in which such circumscribed collections had formed in the posterior fossa and were mistaken for acoustic tumors. In 1924 Horrax⁷ described cases of such collections of fluid, he concluded that they represented chronic adhesive or cystic

¹ Marie, P. Sur deux cas d'acromégalie, *Rev de med* 6 297 (April) 1886, in *Travaux et mémoires*, Paris, Masson & Cie, 1926, vol 1, pp 185-223

² Babinski, J. Tumeur du corps pituitaire sans acromégalie et avec arrêt du développement des organes génitaux, *Rev neurol* 8 531-532, 1900

³ Cushing, H., and Eisenhardt, L. Meningiomas Arising from the Tuberculum Sellae, *Arch Ophth* 1 1-41 (Jan), 168-206 (Feb) 1929

⁴ Holmes, G. Suprasellar Tumors, *Tr Internat Cong Ophth*, 1929

⁵ Cushing, H. The Chiasmatic Syndrome of Primary Optic Atrophy and Bitemporal Field Defects in Adults with a Normal Sella Turcica, *Arch Ophth* 3 505-551 (May), 704-735 (June) 1930

⁶ Schlesinger, H. Beiträge zur Klinik der Rückenmarks- und Wirbeltumoren, Jena, G. Fischer, 1898

⁷ Horrax, G. General Cisternal Arachnoiditis Simulating Cerebellar Tumors, *Arch Surg* 9 95-112 (July) 1924

arachnoiditis and were the sequel of a meningoencephalitis which had left more or less circumscribed areas of adhesions between the arachnoid and the underlying patch of atrophied cortex. The next step came when it was realized that the anterior or chiasmic cistern could also be the site of such pockets; again, one comes to Cushing's paper, published in 1930, in which he stated that if localized meningeal reactions can be produced in the cerebellopontile cistern by an inflammatory process in the middle ear, there is no reason that a similar process might not occur in the chiasmic cistern as a consequence of infection of the paranasal sinuses.

A third line of approach was followed by investigators who were more concerned with lesions of the optic nerves than those of the chiasm and had hoped that operation might relieve mechanical pressure or stricture in some cases. It was evidently this hope which prompted Balado to operate on a patient with bilateral primary optic nerve atrophy. A temporofrontal opening disclosed a milky appearance of the arachnoid, and the thickening of the arachnoid continued as far as the base and surrounded both optic nerves. Balado opened the thickened sheaths of the nerves and observed that they were thinned and abnormally pink. There was improvement of the field, and he and Satanowsky⁸ reported the history of this patient in March 1929.

That year, 1929, was therefore a turning point, or one might say a point of convergence. From that time attention was focused on the possibility of the occurrence of such a case, and many were verified at operation. The papers published by Deery⁹ and Frazier,¹⁰ in 1930, and by Heuer and Vail,¹¹ Davis¹² and Craig and Lillie,¹³ in 1931, are important landmarks in American medical literature. Since 1931, Vincent and his associates,¹⁴ in France, have con-

8 Balado, M., and Satanowsky, P. Tratamiento quirúrgico de la atrofia de la papila, Arch argent de neurol. **4** 71-75, 1929.

9 Deery, E. M. Syndromes of Tumors of the Chiasmal Region, J. Nerv & Ment Dis. **71** 383-396, 1930.

10 Frazier, C. H. Cerebral Pseudotumors, Arch Neurol & Psychiat. **24** 1117-1132 (Dec) 1930.

11 Heuer, G. J., and Vail, D. T. Jr. Chronic Cisternal Arachnoiditis Producing Symptoms of Involvement of the Optic Nerves and Chiasm, Arch Ophth. **5** 334-349 (March) 1931.

12 Davis, L. Chiasmal Syndrome in Intracranial Tumors, Arch Ophth. **6** 181-210 (Aug) 1931.

13 Craig, W. M., and Lillie, W. I. Chiasmal Syndrome Produced by Chronic Local Arachnoiditis, Arch Ophth. **5** 558-574 (April) 1931.

tributed repeatedly to knowledge of this syndrome, and numerous papers have been published in many countries.¹⁵ Two points have gradually emerged as important. First, the field defects were not necessarily bitemporal, and, second, the visual impairment was often due not only to the meningeal lesions and consequent pressure on the optic nerves and chiasm but, to a great extent, to an inflammatory process in the visual pathway itself.

If I were to give my definition of optochiasmic arachnoiditis as I understand it today, I should say that in some cases, as a consequence of various infectious and possibly toxic noxae, a localized inflammatory process can be seen at the base of the brain which affects the chiasm and the optic nerves, as well as the meninges which surround them. The meningeal reaction can take different forms: veins, fibrous bundles, thickened sheaths and circumscribed collections of fluid. Although the meningeal lesions are the most apparent, the inflammatory changes in the underlying visual fibers are often no less essential. The relative importance of the meningeal and the nerve lesions is variable, this may have a bearing on the clinical picture, and possibly on the prognosis. The visual disturbance is not necessarily of the bitemporal type; central scotoma is frequent. In some cases, but in some only, operation will prove useful, but one is not able at present to select such cases. Knowledge is still in a state of flux, and it is likely that this syndrome will eventually be broken down as the etiologic factors are better understood and more is learned about the indications for surgical treatment.

FREQUENCY

Statistical data do not give a true picture, since this disease is not widely known and its existence as an entity is not universally accepted. Some ophthalmologists and surgeons may see a greater number of cases than is normal because they are particularly interested in the syndrome. Others have failed to recognize the condition or have treated it with nonoperative procedures.

14 (a) Vincent, C., David, M., and Puech, P. A propos de sept cas d'arachnoidite opto-chiasmatique, Rev neurol. **1** 760-767, 1931. (b) Vincent, C. Le traitement chirurgical des compressions directes du chiasma et du nerf optique dans le crâne, Bull Soc d'opht de Paris, 1932, pp. 282-301. (c) Vincent, C., Puech, P., and Berdet, H. Les arachnoidites de la base du cerveau, Rev d'oto-neuro-opht. **14** 417-428, 1936.

15 (a) Malbran, J., and Balado, M. Arachnoiditis quiasmatica, Arch argent de neurol. **8** 96-106, 1933. (b) Morea, R. Tratamiento quirúrgico de la atrofia de la papila, ibid. **7** 301-331, 1933. (c) di Maizio, Q., Cavina, C., and di Negris, G. Sulla arachnoidite opto-chiasmatica, Riv oto-neuro-oftal. **13** 291-328, 1936.

so that the diagnosis has not been verified. With these reservations, the following figures are cited. In 1930 Deery⁹ stated that of 170 cases of chiasmic and perichiasmic tumors and pseudo-tumors operated on in Cushing's service during the preceding ten years, 13 had been cases of optochiasmic arachnoiditis. In 1931 Heuer and Vail¹¹ found that in 5 per cent of 43 cases of optic nerve atrophy the condition was due to optochiasmic arachnoiditis. In 1938, when I was working in the ophthalmologic department of Vincent's neurosurgical service I published, with Guillaumat,¹⁶ a statistical report of all verified cases in which the eyes had been examined either in that department or in my private practice. My findings follow:

	No of Cases
All intracranial tumors including those of the chiasmic region	847
Tumors of the chiasmic region	
Pituitary adenoma	50
Cranipharyngioma	37
Tumors of the chiasm	16
Other tumors	6
Total	109
Circumscribed pockets of serous meningitis on the outer surface of the hemispheres	48
Arachnoiditis of the posterior fossa	35
Optochiasmic arachnoiditis	78

These figures show that optochiasmic arachnoiditis is not a rare disease, but the relative proportion is certainly too high, as previously stated, since Vincent and his co-workers were particularly interested in this disease. In 1937, Bollack, David and Puech,¹⁷ the last two also associates of Vincent, published a book on optochiasmic arachnoiditis.¹⁸ At that time they had found 63 reported cases, and they added to these 66 more previously unreported cases, making a total of 129 cases. These cases should not be added to those given in the tabulation, as many of the same cases are counted in the two series.

Optochiasmic arachnoiditis is more frequent in adult life, 60 per cent of cases occur between the ages of 20 and 40, with a maximum between the ages of 20 and 30. The findings of Bollack, David and Puech¹⁷ follow:

16 Hartmann, E., and Guillaumat, L. Aspect du fond d'œil dans les tumeurs intracraniennes, Ann d'œil 75:717-737, 1938.

17 Bollack, J., David, M., and Puech, P. Les arachnoïdites optochiasmatiques, Paris, Masson & Cie, 1937.

18 I have made considerable use of this book not only because it is the most complete survey of optochiasmic arachnoiditis but because I had personally examined most of the patients forming the material of this work.

	No of Cases
Between birth and 10 years of age	7
From 10 to 20	12
20 to 30	37
30 to 40	35
40 to 50	27
Over 50	6
	<hr/>
	124
Men affected	77
Women affected	46
	<hr/>
	123

PATHOLOGIC FEATURES

To facilitate the description of the lesions encountered, one may, rather artificially, separate them into three types: thickening and adhesions of the arachnoid, circumscribed collections of fluid, and atrophy of the optic nerves and chiasm. One should, however, bear in mind that any one of these three types of lesions rarely occurs alone but merely predominates and that the relative proportion is variable.

1 *Thickening of the Arachnoid and Adhesions*—The arachnoid is thickened and encases the optic nerves and the optic chiasm more or less completely. It forms adhesions both with the visual pathway and with the surrounding organs, in particular the cortex, the olfactory nerves and the perichiasmic blood vessels (internal carotid, anterior cerebral, anterior communicating and ophthalmic arteries). There is notable vascularization of the thickened arachnoid. The veins are sometimes extremely dilated, pointing to impairment of the return circulation. Occasionally one sees small calcareous deposits. The arachnoid sometimes forms a continuous milky veil or a heavy membrane. In other cases innumerable short, fine, cobweb-like adhesions are attached to the chiasm and the optic nerves. In other cases strong, thick fibrous bundles bridge the perichiasmic region, most of these seem to originate from the neighboring arteries, the internal carotid and the ophthalmic artery in particular, and in many cases they form strictures of the optic nerves and the optic chiasm, which may be deeply grooved. Such strictures may also be due to the fact that the anterior cerebral or the anterior communicating artery is drawn away from its normal course and bound down by arachnoid adhesions.

2 *Circumscribed Pockets of Subarachnoid Fluid*—Circumscribed pockets of serous meningitis in the perichiasmic region may closely simulate a tumor both in their appearance and in the way

they bring pressure on the visual pathway. The pocket is suprasellar, and usually above and anterior to the chiasm, but it has sometimes been seen under the chiasm and the optic nerves. In other cases there is not one large pocket but innumerable small ones.

Atrophy of the Visual Fibers—The optic nerves and optic chiasm are rarely normal. They usually show more or less pronounced atrophy, the nerves, in particular, may be reduced in caliber and in some instances flattened. Less frequently one may see enlarged optic nerves, giving the impression of being edematous and appearing to be strangulated at the optic foramen. Their color is rarely normal, being at times grayish white, sometimes of a gelatinous appearance, and at other times notably congested, with excessive vascularization of the surface. While in some cases the atrophy of the visual pathway seems to be a consequence of the constrictions exerted by the thickened arachnoid or by a pseudotumorous pocket of serous meningitis, in other cases the meningeal lesions are so discrete and the atrophy of the optic nerves so pronounced that one has the impression, rather, of a primary inflammatory process of the nerves.

There are few satisfactory reports of the microscopic lesions. Davis and Haven¹⁹ in 2 cases noted that there were prominent thickening of the reticular structure, due to an increase in the fibrous elements, and a moderate amount of leukocytic infiltration of this reticular area. Bollack, David and Puech¹⁷ reported 2 cases in which the optic nerves and optic chiasm were examined. There was peripheral neuritis with demyelination and atrophy of some of the more superficial nerve fibers.

ETIOLOGIC FACTORS

It has long been known that in some cases a localized area of arachnoiditis may cover an underlying tumor, and this may occur in the chiasmic area, as well as on the outer surface of the hemispheres, but I shall not discuss this type of peritumoral arachnoiditis here.

In the present state of knowledge no one etiologic factor is evident. Rather, one gathers the impression that optochiasmic arachnoiditis can be caused by several infectious, and possibly some toxic, noxae. The most comprehensive statistics are those cited by Bollack, David and Puech¹⁷. I have tabulated the etiologic agents suspected in the 63 cases reported in the litera-

ture prior to their publication and the causal factors in the 66 previously unpublished cases which they reported. The second group of cases is more interesting, as a possible etiologic agent was found in a greater percentage of cases than in the first group.

	Previously Published Cases	Unpublished Cases	Total No of Cases
Total no of cases	63	66	129
Total no of possible causes found	28	53	81
Trauma of the skull or orbit	9	10	19
Diseases of the nose, sinuses and tonsils	7	10	17
Syphilis	3	9	12
Otitis	2	4	6
Tuberculosis	1	4	5
Familial disease	1	3	4
Rheumatic fever	0	3	3
Teeth	2	0	2
Encephalitis	1	1	2
Pregnancy	1	1	2
Influenza	0	2	2
Infection with colon bacillus	0	2	2
Herpes zoster (intercostal)	0	1	1
Cerebrospinal meningitis	1	0	1
Typhus	0	1	1
Diabetes	0	1	1
Erysipelas	1	0	1
Alcoholism	0	1	1
Mumps	1	0	1

One should bear in mind that this classification is only tentative, and an infectious disease reported in the patient's history previous to his visual disturbance implies no certainty as to its causative action. In several cases two possible causes were reported, such as infection of the teeth and nose, infection of the nose and sinuses, infection of the sinuses and trauma, tuberculosis and trauma and nasal infection and otitis. Some of these etiologic possibilities should be considered more carefully, namely infections of the sinuses and nose, trauma and syphilis.

Infection of the Nose and Sinuses—When reporting one of the first cases in 1929, Cushing⁵ stated:

That a mild meningeal reaction may be produced in the cerebellopontile cisterna by an inflammatory process in the middle ear with symptoms suggesting those of an acoustic tumor, is well known. There is no reason why a similar process might not occur in the chiasmal cisterna in association with inflammatory processes in the accessory paranasal sinuses [page 730].

Such an etiologic factor was also accepted as probable by Monier-Vinard,²⁰ by Puech, David

¹⁹ Davis, L., and Haven, H. L. Pathologic Study of the Intracranial Arachnoid Membrane, *J. Nerv. & Ment. Dis.* 73:129-143 and 286-300, 1931.

²⁰ Monier-Vinard, M., in discussion on Puech, P., David M., and Brun, M. *Rev d'oto-neuro-ophth.* 11: 621, 1933.

and Brun²¹ and by Vail²². In 1936 Worms²³ reported an interesting case history. His patient had a long-standing infection of the sphenoid sinuses with polyps, and osteitis of the posterior wall, a perforation occurred eventually, and the patient died. Postmortem examination disclosed conspicuous perichiasmic arachnoid membranes. But this is a rather unusual occurrence. More often the symptoms are less acute, and only a relatively moderate and subacute or chronic inflammatory process is seen. Also, the initial infection need not be in the sinuses, a chronic infection of the postnasal cavity or of the tonsils may be a sufficient cause. The lymphatic channels of the nose are known to be directly related to the subarachnoid spaces, and there is also an anastomosis linking the veins of the sphenoid sinuses and the ethmoid cells to the ophthalmic veins and to small veins originating in the dural sheaths of the optic nerve in the optic canal. Either of these channels might be responsible for inflammatory arachnoiditis, even without fissures of the bones. Infections of the nose and sinuses are so frequent, however, that arachnoiditis may well occur in a patient previously a victim of such trouble without this being the real cause.

Trauma—It is usual for a patient to find a traumatic explanation for almost any disease, and more or less severe trauma to the head is so frequent an occurrence, even with normal people, that such a history in the case of a patient with arachnoiditis is not necessarily significant. Some cases, however, are suggestive in particular, the case reported by Weill,²⁴ in which symptoms of adenoma of the pituitary were present and operation, performed by Vincent, revealed optochiasmic arachnoiditis, with fibrous tracts starting from the vault at the site of a scar of the epineurium and the skin. The patient had previously had an automobile accident, resulting in an injury to the head. In 1 of the first cases reported, case 1 of Holmes,⁴ there had been a trauma to the skull, and in several other cases the condition has been ascribed with more or less certainty to a head injury (Malbran and Baldado,^{15a} Morea,^{15b} di Marzio, Cavina and di Negris,^{15c} Heuer and Vail,¹¹ and others).

Bollack, David and Puech¹⁷ found 10 cases of head trauma in their series of 66 cases of this

21 Puech, P., David, M., and Brun, M. Contribution à l'étude des arachnoidites opto-chiasmatiques, Rev d'oto-neuro-ophth **11** 641-649, 1933.

22 Vail, D. Optochiasmatic Arachnoiditis, Arch Ophth **20** 384-394 (Sept) 1938.

23 Worms, G. Syndrome oculo-hypophysaire consécutif à une sinusite sphénoidale suppurrée, Arch d'ophth **53** 207-217, 1936.

24 Weill, G., in discussion on Les arachnoidites opto-chiasmatiques, Bull et mem Soc franç d'opht **54** 198, 1937.

form of arachnoiditis, and in 6 cases the trauma was the only likely etiologic factor, in 4 cases other causes were present (syphilis, tuberculosis and nasal or sinal infection). In 1939 Kenel²⁵ reported 5 cases of optochiasmic arachnoiditis of traumatic origin, in 4 of which operation was performed.

It is evident, therefore, that a head trauma must be accepted as a possible cause of optochiasmic arachnoiditis, and this may have important legal implications. If the arachnoiditis followed shortly the head injury, the link is evident, but the visual disturbance may be a late symptom, and in such cases doubt may persist, especially if the trauma was moderate or if some other possible etiologic factor is present, such as syphilis or sinusitis.

Syphilis—There is no general agreement as to the part played by syphilis. A priori reasoning might lead one to accept this type of infection as a frequent cause since one knows how often chronic meningitis with optic nerve atrophy follows insufficiently treated syphilis. However, cases of this type are more usually classified with tabes, and the condition differs from the disease I am discussing in this review. But it is certain that patients with optochiasmic arachnoiditis sometimes have a history of syphilis.

In Cushing's first case⁵ (1929) the serologic reaction was suspected of being positive, and similar cases have been reported by François,²⁶ MacPherson²⁷ and Schaub²⁸. In 1936 Vincent Puech and Berdet^{14c} claimed that in 2 out of 5 of their cases the Wassermann reaction of the blood was positive. Of their 129 cases, Bollack, David and Puech¹⁷ reported on the Wassermann reaction of the blood in only 78. It was positive in 12 and negative in 66 cases, the Kahn reaction being positive in 1 of the latter. Hausman²⁹ especially stressed the importance of syphilis in arachnoiditis. In 1937 he reported 5 cases, and in 1940 he gave his observations in 15 cases of syphilis and diseases of the optic nerves occurring

25 Kenel, C. Five Cases of Traumatic Optochiasmic Arachnoiditis, *Ophthalmologica* **96** 345, 1939, abstracted, Am J Ophth **22** 811, 1939.

26 François, J. Arachnoidite optochiasmatique syphilitique et pyretotherapie, Bull et mem Soc franç d'opht **50** 185-189, 1937.

27 MacPherson, W. A. Chiasmal Arachnoiditis, Am J Ophth **23** 1275-1276, 1940.

28 Schaub, C. F. Syphilitic Optico-Chiasmatic Arachnoiditis, Am J Ophth **24** 1313, 1941.

29 Hausman, L. Syphilitic Arachnoiditis of the Optic Chiasm, Arch Neurol & Psychiat **37** 929-958 (April) 1937, Syphilitic Atrophy of the Optic Nerves and Papilledema Due to Optochiasmatic Arachnoiditis Indications for Surgical Intervention, Arch Ophth **23** 1107-1115 (May) 1940, The Surgical Treatment of Syphilitic Optic Nerve Atrophy Due to Chiasmal Arachnoiditis, Am J Ophth **24** 119-132, 1941.

in the service of Dr. Foster Kennedy: 1 case of papilledema, 1 case of secondary optic nerve atrophy and 13 cases of primary optic nerve atrophy. In 4 cases the chiasmatic region was explored, 3 being cases of the primary type of optic nerve atrophy and 1 a case of secondary optic nerve atrophy. In the first 3 cases adhesions were present around the chiasm, these were removed, and vision improved. The patient with secondary optic nerve atrophy had internal hydrocephalus, and his condition did not improve.

My associates and I¹⁶ have reported the history in a case of tabes with altitudinal hemianopsia, an unusual complication of this disease; operation disclosed that a thick veil of arachnoid adhesions had pulled the anterior cerebral artery away from its normal course and bound it down against the superior aspect of the chiasm, which was deeply grooved. That syphilis plays a part in the causation of optochiasmic arachnoiditis is certain, but arachnoiditis is far from being due to syphilis in all cases, and operation should not be performed in all cases of optic nerve atrophy complicating syphilis. In this matter the ophthalmologist should use his judgment.

One should also bear in mind that in a syphilitic patient, even with a positive Wassermann reaction of the blood, arachnoiditis may be due to some other cause. Of the 12 cases in which Bollack, David and Puech¹⁷ reported a positive Wassermann reaction of the blood, a dental infection was also present in 1, diabetes in 1, trauma to the frontal area in 1 and chronic nasal infection in 2. Arachnoiditis in a syphilitic patient is not necessarily of syphilitic origin.

MECHANISM OF THE VISUAL SYMPTOMS

When the first cases of optochiasmic arachnoiditis were reported, it was considered evident that the optic chiasm and the optic nerves suffered from direct pressure, that circumscribed collections of fluid acted as would a solid tumor and that thickened membranes or fibrous bundles were noxious because of constriction of the visual fibers. Such an explanation is still accepted in a great number of cases, but it has gradually become apparent that it did not suffice in a series of other cases. Pressure on or constriction of the optic nerves and chiasm is sometimes of moderate degree, in contrast to the abnormal, and often atrophic, appearance of the nerves. The importance of the inflammatory process in the visual pathway has been increasingly emphasized, and the present tendency is to con-

sider optochiasmic arachnoiditis not as a disease of the arachnoid, with secondary mechanical damage to the nerve fibers, but as an inflammatory process involving the arachnoid and the nerve fibers in variable proportions. Some authors have concluded that the inflammatory process occurs simultaneously in the two structures, others have stated the belief that it begins in the meninges and spreads to the optic nerves and the optic chiasm, and some investigators have asserted that it more often originates in the visual pathway and that the arachnoiditis is a secondary reaction.

It cannot be overlooked, moreover, that the visual fibers may suffer from an impaired blood flow. It has often been noted that the arachnoid adhesions exerted a traction on the arteries from which the chiasm and optic nerves derived their supply and that in some patients the veins were notably congested, as though there was an obstacle to the return circulation. The normal nutrition of the nerve fibers might therefore be altered by mechanical ischemia, by a reflex spasm (Sourdille¹¹) or by venous stasis. This venous engorgement is worth noting at a time when there is a tendency to consider multiple sclerosis and the other demyelinating diseases as noninfectious and as due to venous thrombosis (Putnam¹²). Vail²² stated that encephalitis, multiple sclerosis and optochiasmic arachnoiditis were closely allied and might be different manifestations of the same pathologic process, which could well be thrombosis of the venous system of the nerve tissue.

It is reasonably certain that no single mechanism is responsible and that several factors may produce the visual disturbance, either in different patients or in the same patient, the relative importance of these mechanisms being variable.

SYMPTOMS

Field Defects.—In most of the early cases bitemporal field defects were recorded. This was only natural since at first optochiasmic arachnoiditis was usually encountered at operation in cases in which a tentative diagnosis of adenoma of the pituitary or suprasellar tumor had been made. It gradually became evident however, that bitemporal hemianopsia was not the only type of field defect and, in fact, was not even the most frequent.

31 Sourdille, G P. Utilité d'une thérapeutique extracranienne au stade début de l'arachnoïdite, Bull et mém Soc franç d'opht 50:181-184, 1937

32 Putnam, T J. Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," Arch Neurol & Psychiatr 37:1298-1321 (June) 1937, Multiple Sclerosis and Encephalomyelitis, Bull New York Acad Med 19:301-316, 1943

30 David, M., Hartmann, E., and Hebert, E. Arachnoïdite et compression vasculaire du chiasma chez un tabétique, Bull Soc d'opht de Paris, 1936, pp 789-798

In a series of 129 verified cases Bollack, David and Puech¹⁷ noted the following distribution of field defects

	Percentage
Central scotoma	31
Concentric contraction	23
Bitemporal hemianopsia	17
Binasal depression	7
Lateral homonymous hemianopsia	5
Altitudinal hemianopsia	5

In 12 per cent of the cases the fields were normal, they were not mentioned, they could not be charted on account of poor vision or they were so irregular that the authors were unable to classify them

Deery⁹ mentioned central scotoma in 4 of his 13 cases, and Craig and Lillie,¹³ in 4 of their 8 cases. Central scotoma is therefore an essential feature. It is bilateral, usually very large and can be found together with a peripheral contraction of the field.

Concentric contraction was observed by Heuer and Vail¹¹ in 3 of their 4 cases, by Morea^{15b} in 3 of 9 cases and by di Marzio and his co-workers^{15c} in 3 of 7 cases. The field is irregularly depressed and sometimes notably contracted. Sometimes a central scotoma is present. In some cases this irregular contraction predominates on one side, and the field is then classified as one of the following types:

1 Bitemporal field defects are often irregular, and concentric depression of the field is more pronounced on the temporal side. The fields are almost never as regular as with adenoma of the pituitary or a suprasellar meningioma, and the changes do not follow the usual progression, from the temporal superior to the temporal inferior quadrant and then to the nasal inferior and the nasal superior quadrant. A central scotoma is also often present, even at an early stage.

2 A few cases of binasal depression have been reported in association with optochiasmic arachnoiditis and Vincent and I observed 4 instances of this rather unusual field defect.³³ Craig and Lillie¹³ expressed the belief that it was related to a fairly anterior pressure, exerted on the optic nerves rather than on the chiasm.

3 Lateral homonymous hemianopsia, when present, is sometimes complete, and sometimes of only quadrant type. The field defects are usually atypical and incongruous. Craig and Lillie¹³ observed an unusually large proportion of cases

in which they were present 3 out of 8 cases. Deery⁹ noted them in 2 of 13 cases of this form of arachnoiditis. A few more cases have also been reported.

4 Di Marzio, Cavina and di Negris^{15c} observed 4 cases of altitudinal hemianopsia in their series of 7 cases of optochiasmic arachnoiditis, the condition being inferior in 3 cases and superior in 1 case. I have personally observed 1 case of the inferior type, due to pressure of the anterior cerebral artery on the superior aspect of the chiasm.³⁰

Visual Acuity—Contrary to what usually occurs in cases of pituitary adenoma, the visual acuity fails at an early stage of the disease. This loss of vision is bilateral in most cases, but some cases of unilateral loss have been reported. When it is bilateral, one eye is often affected before the other. Visual acuity may fail slowly, as in cases of perichiasmic tumors, but the loss of vision is sometimes rapid, or even sudden, occurring in two weeks in 2 cases of Heuer and Vail,¹¹ in one month in a case of di Marzio, Cavina and di Negris^{15c} and in three months in a case of Cossa.³⁴ Craig and Lillie¹³ concluded that rapid failure of vision was characteristic of this disease.

Fundus—The disk is rarely normal, at least at the stage at which the patient is usually examined. In a series of 129 verified cases, Bollack, David and Puech¹⁷ noted the following distribution of changes:

	Percentage
Primary optic nerve atrophy	38
Optic nerve atrophy with blurred margins	16
Papilledema	10
Temporal discoloration	7
Hyperemia of the disk	7
Altitudinal atrophy	4
Normal disk	10
Unclassified	8

Di Marzio, Cavina and di Negris^{15c} noted atrophy either of the lower or of the upper half of the disk. The other half of the disk showed slight edema, and in all the cases altitudinal hemianopsia was present. Vail²² asserted that the appearance of an atrophy which lies between the primary and the secondary type of atrophy was highly suggestive of arachnoiditis, and such has been my own experience.

Other Symptoms—Symptoms other than visual disturbances are unexpectedly rare. A few, but only a few, cases have been reported in which oculomotor or abducens paralysis,

³³ Vincent, C., and Hartmann, E. Douze observations de rétrécissement binasal du champ visuel au cours d'affections intracraniennes, Ann d'œil **171** 193-207, 1934.

³⁴ Cossa, P. Cecité par nevrite optique, intervention sur la région opto-chiasmatique, Rev d'oto-neuro-ophth. **11** 441-444, 1933.

nystagmus, trigeminal anesthesia and pupillary inequality were present, then scarcity showing how localized the arachnoiditis usually is.

Headache is more frequent and is noted in about one third of all cases. The pain is usually frontal, in other cases it is localized behind the eyes, and it often radiates to the neck and shoulder. This is an early symptom and often appears before there are any visual disturbances. Drowsiness is sometimes also present, with moderate elevation of temperature, nausea and dizziness. These symptoms are usually temporary and may have disappeared when vision fails and the patient is first examined.

Few patients have other neurologic symptoms, such as anosmia, facial paralysis, auditory and vestibular disturbances, polydipsia, polyuria, obesity and dyspituitarism.

The spinal fluid is usually normal. In a few patients there was a moderate increase in the protein content or of the cell count.

Röntgenographic Evidence—Roentgenologic studies are helpful in that they show none of the signs usually found with sellar or suprasellar tumors. The sella is not enlarged, as with adenoma of the pituitary. In exceptional cases an infrachiasmatic pocket of serous meningitis may give the picture usually observed in cases of glioma of the optic chiasm or of the optic nerves. Puech³⁵ reported such a case in which both optic foraminae were enlarged and in profile the sella was Ω shaped. Ryan³⁶ observed destruction of the bone in the posterior wall of the optic canal on one side. Calcareous deposits have been observed in exceptional cases (François³⁷). Opacity of the sinuses is frequently noted, and in some cases a shadow extends to the base of the skull in the middle fossa. Hirtz and Worms³⁷ stressed the value of this sign in cases of "perisinusitis."

Air studies usually prove the ventricles to be of normal size and location, in some cases they are even reduced in size (Vincent, David and Puech³⁸). Encephalography was found useful by Lillie³⁹. The chiasmatic cistern is irregular and deformed. Compensatory channels are apparent in the frontal and occipital poles, and there is interference at the vertex with the normal path-

ways of the subarachnoid fluid. Slight cortical atrophy is suggested. The essential feature is the absence of evidence of a space-taking lesion within the cranium. Fay⁴⁰ noted that stereoscopic encephalograms sometimes revealed adhesions in the chiasmatic region.

DIAGNOSIS

From the preceding discussion one realizes that optochiasmatic arachnoiditis is polymorphous and that the diagnosis cannot be approached in the same way in all cases.

In some cases the temporal field defects suggest pressure on the chiasm, and therefore the presence of a sellar or a suprasellar tumor. But with arachnoiditis the bitemporal depression is usually not exactly the same as with such tumors. It is less regular both in pattern and in growth. In most cases a more or less concentric contraction predominates on the temporal side of each field. With intrasellar tumors (adenoma of the pituitary and intrasellar craniopharyngioma) there are more symptoms of dyspituitarism, and the sella appears enlarged in a profile roentgenogram. A suprasellar tumor, such as a meningioma of the tuberculum sellae or a meningioma lying in the very posterior part of the olfactory groove should also be considered, however, such a tumor usually comes into view in air ventriculograms, and in some cases the tuberculum sellae gives an abnormal picture both in the antero-posterior and in the lateral roentgenogram. Suprasellar craniopharyngioma is often detected by a roentgenogram or an air encephalogram and is usually more noticeably associated with symptoms of hypothalamic and infundibular involvement. The tumor also occurs at an earlier age. Glioma of the chiasm may offer difficulty in differential diagnosis, since the field defects are fairly similar and pockets of serous meningitis may sometimes give a roentgenographic picture somewhat like that of glioma. Fortunately, gliomas are met mostly in children, who rarely have arachnoiditis. Moreover, other symptoms of Recklinghausen's disease are sometimes present and are then helpful. Bitemporal field defects may also accompany nontumoral diseases, such as multiple sclerosis, encephalitis and Roenne's⁴¹ chiasmatic form of retrobulbar neuritis, but with these diseases the visual disturbances are more often of a different type, as I shall indicate later.

The diagnosis is approached differently if the patient has bilateral optic nerve atrophy with a

35 Puech, P., in Bollack, David and Puech,¹⁷ pp 49 and 130.

36 Ryan, E. R. Optochiasmatic Arachnoiditis, Arch Ophth **29** 818-825 (May) 1943.

37 Hirtz, E. J., and Worms, G. Des "perisinusites" profondes, leur image radiologique, Ann d mal de l'oreille **45** 833 (Sept.) 1926.

38 Vincent, C., David, M., and Puech, P. Sur la ventriculographie, Rev neurol **40** 1031-1096, 1933.

39 Lillie, W. I. Prechiasmal Syndrome Produced by Chronic Local Arachnoiditis, Arch Ophth **24** 940-947 (Nov.) 1940.

40 Fay, T., in discussion on Lillie³⁹.

41 Roenne, H. Ueber akute Retrobulbarneuritis im Chiasma lokalisiert, Klin Monatsbl f Augen **55** 68-97, 1915; On Nonhypophyseal Affections of the Chiasma, Acta ophth **6** 332-343, 1928.

concentric and more or less regular contraction of the field. A few features are at once suggestive of arachnoiditis: bilateral involvement of the eyes, the presence sometimes of a central scotoma and frequent slight edema superimposed on the primary optic nerve atrophy. In most cases infectious optic neuritis does not produce a similar picture, in very few cases is this condition bilateral. Syphilis is more likely to be considered in the form either of chronic syphilitic meningitis or of tabes. The diagnosis of the former condition is not always easy, or even possible, since syphilis may in some cases be the cause of arachnoiditis. It is a moot point to decide how frequently syphilis is an etiologic factor and whether and when surgical intervention is advisable. The optic nerve atrophy of tabes is more easily diagnosed, but some authors have questioned whether operation might not sometimes be helpful in cases of this condition. I had an operation performed in a case of this type, although the patient had tabes, a rapidly failing vision and altitudinal hemianopsia made me wonder whether there was not an arachnoid stricture which could be removed. I have already referred to this case. The point is not to make a diagnosis of arachnoiditis from chronic syphilitic meningitis and from tabes, but rather to determine in which cases tabes and meningitis may benefit from surgical treatment. Such cases are rare, but more may be learned about them in the future. In syphilitic patients treated with pentavalent arsenic bilateral toxic neuritis with peripheral contraction of the fields must occasionally be considered.

It is in cases of the type with bilateral central scotoma that diagnosis is the least easy. Toxic amblyopia, with bilateral central defects due to intoxication with such substances as alcohol, tobacco, lead, thyroid and carbon disulfide, is usually readily recognizable from the history. Moreover, the central scotoma of arachnoiditis is larger and irregular in shape, and there is often a peripheral contraction. Most infectious optic neuritis is unilateral, whether due to syphilis, sinus disease or other focal infection. It is only when both optic nerves are affected that one considers arachnoiditis. Here, again, when a sinus infection or syphilis causes a bilateral central scotoma it is not easy to differentiate the two conditions, since both diseases can cause arachnoiditis, and one is usually more concerned with the advisability of a chiasmic exploration than with a purely academic diagnosis. Multiple sclerosis, Devic's disease (optic neuro-encephalomyopathy) and disseminated encephalitis, especially the first two conditions, are

more likely to affect both optic nerves. The diagnosis is difficult when the visual symptoms appear before all others. Such is sometimes the case with multiple sclerosis, but the optic neuritis is then usually acute or subacute, in contrast to the chronic course of arachnoiditis. It is only in the less frequent cases in which bilateral slowly progressive optic nerve atrophy appears as an initial symptom of multiple sclerosis that the diagnosis is difficult. Roenne's chiasmic retrobulbar neuritis is not universally accepted and is rare in any case. Spinal symptoms are often present, the evolution is subacute, and field defects are changeable. It is possible that a majority of cases of this condition would now be classified with the demyelinating diseases and that in some instances arachnoiditis may have been present. Leber's disease (hereditary optic atrophy) should be easily recognized, with its history of familial optic nerve atrophy. It should be noted, however, that in some cases of this disease operations revealed optochiasmic arachnoiditis. Davis and Haven¹⁹ reported such a case, and Vincent and his associates have operated in 4 other instances.¹⁷ Such facts are disturbing.

TREATMENT

If any possible cause is found, such as sinus infection, syphilis or rheumatic fever, therapeutic measures are self evident. They should not be continued, however, without discretion, and if the arachnoiditis does not respond within a reasonable time and the visual disturbances continue to increase, operation should be considered.

Even if no evident etiologic factor is found, nonoperative treatment is advisable within normal time limits. Several forms of medication, such as intravenous injections of sodium salicylate, sodium iodide, mercuric cyanide, methenamine and thiamine chloride, use of neurotropic vaccines and nonspecific protein therapy, have been advocated, but none has proved effective. Semipenetrating roentgen radiation should also be applied, and this treatment can be employed while some of the preceding forms of medication are being tried. If there is no improvement, especially if vision continues to fail and the field becomes more defective, surgical intervention should not be delayed too long.

The chiasmic region can now be explored with but slight mortality, and one is entitled to take some risks if all other procedures have failed and blindness is to be feared. In 1936 Vincent, Puech and Berdet^{14c} reported on a series of 95 operations, with 7 deaths. Three of the deaths

occurred among the first patients to be operated on and the technic was eventually improved. Of the other 4 patients, 1 was aged and died of bronchopneumonia a few days after the operation.

The visual results are far from being as favorable as those which follow removal of a tumor. Statistics vary considerably which is to be expected as the series are short and most of the reports are incomplete. The largest complete series is that from the Pitie Hospital in Paris reported by Bollack, David and Puech.¹⁷ Of these 66 cases, improvement occurred in 19 (28 per cent) and the result of the operation was doubtful or poor in the other 47 cases. Of the 63 cases previously reported by several neurosurgeons and collected by Bollack, David and Puech improvement occurred in 29 (46 per cent). It is difficult to know whether the notable difference between the two figures is due to the fact that most of the previously reported cases

were the favorable ones, to a difference in surgical technics, or to the willingness of Vincent and his co-workers, at the Pitie Hospital, to attempt surgical treatment even in the most hopeless cases.

It is not clear at present whether the cystic or the adhesive type carries the best prognosis for visual improvement. Strangely, the appearance of the optic nerves is not a sure guide, except, of course, in cases of extreme atrophy. There is unfortunately, no standard by which one can form any judgment, before operation, of which patients should be operated on and may improve and which will not respond to surgical treatment. Even conditions of long standing have improved to a certain extent but on the whole results have been far better when operation was done in the early stages of the disease.

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PARESIS OF RIGHT SUPERIOR OBLIQUE AND OF LEFT SUPERIOR RECTUS MUSCLE DIFFERENTIAL DIAGNOSIS

To the Editor —In January 1938 Dr Alfred Bielschowsky, then director of the Dartmouth Eye Institute, delivered ten lectures before the Los Angeles Research Study Club on motor anomalies of the eyes. The eighth and ninth lectures had previously been published in this journal (Lectures on Motor Anomalies of the Eyes II Paralysis of Individual Eye Muscles, ARCH OPHTH 13: 33 [Jan], IV Functional Neuroses Etiology, Prognosis and Treatment of Ocular Paralysis, ibid 13: 751 [May] 1935). Most of this material is republished in the November 1944 issue of the ARCHIVES, page 372, as the text for a paper by Dr William Thornwall Davis, entitled "Paresis of Right Superior Oblique and of Left Superior Rectus Muscle Differential Diagnosis".

In this country ophthalmologists with few exceptions have accepted the views of Dr Alexander Duane concerning the differential diagnosis of vertical motor anomalies. His opinions have been popularized by Dr James W White, at the New York Post-Graduate Medical School and Hospital, where I have been on the faculty for twenty-five years. Since the publication of Bielschowsky's lectures two years ago, my colleagues and I have observed that ophthalmologists from the West Coast in our eye muscle courses feel strongly with Bielschowsky that "by far the most frequent and important type of paralysis of a simple vertical motor anomaly is trochlear nerve palsy." Dr Davis reports that

"of 88 cases of paresis of the superior oblique and the superior rectus muscle, the superior oblique was involved in 48, or 54.5 per cent, and the superior rectus in 40, or 45.5 per cent." In sharp contrast are the results of an exhaustive clinical study of 527 cases by Dr J W White and Dr Harold W Brown (Occurrence of Vertical Anomalies Associated with Convergent and Divergent Anomalies, ARCH OPHTH 21: 999 [June] 1939), with the superior oblique muscle involved in 20 cases, or 4 per cent, and the superior rectus muscle in 507 cases or 96 per cent. It is not possible that these authorities overlooked about 50 per cent of their cases with involvement of the superior oblique.

Publication of Dr Davis' paper once more revives the dormant Bielschowsky-Duane argument and, unfortunately, will create confusion in the minds of the younger ophthalmologists. Although Dr White remarked in his discussion on Dr Davis' paper (page 379) that "in 1914, Bielschowsky never convinced Duane,

Duane never convinced Bielschowsky, [and] Dr Davis has not convinced me," I trust that the brilliant and lasting contributions of Bielschowsky will never again be clouded by conflicting opinions on one small aspect of his voluminous research.

In the hope that this time-worn controversy will be settled, I suggest that the Section on Ophthalmology of the American Medical Association, at its Philadelphia meeting in June 1945, appoint a committee to standardize the differential diagnosis of paralysis of the superior oblique and of the superior rectus muscle.

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Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Conjunctiva

INCLUSION BLENNORRHEA J H ALLEN Am J Ophth 27: 833 (Aug) 1944

Allen divides this article into two sections, the first giving the data on 43 cases of inclusion blennorrhea with respect to incidence, seasonal variation, cause and manifestations. In the second section he found that, contrary to Lindner's suggestion, in a series of 43 consecutive conjunctival passages the etiologic agent of inclusion blennorrhea did not change its disease-producing characteristics or progressively alter its virulence.

W S REESE

UNILATERAL MEMBRANOUS CONJUNCTIVITIS WITH COMPLETE CAST J F GALPINE and D R CAMPBELL, Brit J Ophth 28: 412 (Aug) 1944

In a girl aged 6 years the ocular condition developed during an attack of scarlet fever, complicated by vulvovaginitis. Smear of material from the eye showed a large number of gram-negative diplococci, both intracellular and extracellular, which were indistinguishable from gonococci. The latter were never obtained in culture. The appearance was that of membranous conjunctivitis. The report on the culture indicated that the infection was streptococcal. In its development the membrane almost hid the cornea and extended from the limbus as a complete lining throughout the conjunctival sac. About one month from the onset the membrane came away as a complete cast.

W ZENTMAYER

LYMPHOCYTOSIS AND ITS SIGNIFICANCE IN EYE DISEASES S V OAK, Indian J Ophth 4: 78 (Oct) 1943

Oak discusses the origin of lymphocytes and points out that they play an important part in chronic inflammatory processes of the eye. He gives a clinical description of the conjunctival conditions of which they are an important histologic feature.

Congenital Anomalies

CONGENITAL FOLDS OF THE RETINA A VAZQUEZ BARRIERE and L A BOADO Arch de oftal de Buenos Aires 18: 572 (Nov) 1943

This malformation consists in a crease of the retina, forming a fold above the retinal plane, always beginning at the papilla and spreading

toward the periphery in fan fashion. Frequently the peripheral end extends beyond the limits of the ophthalmoscopic field, reaching the ciliary body, and even the equator of the crystalline lens.

Only four important papers on this condition have appeared thus far, and up to the time of writing only 40 cases have been reported in the literature.

The authors describe 2 cases illustrating this rare condition.

H F CARRASQUILLO

Cornea and Sclera

INFRA-RED THERAPY OF FLASH KERATOCONJUNCTIVITIS D G COGAN V E KINSEY and P DRINKER, J A M A 123: 883 (Dec 4) 1943

The authors supply the following summary:

"Keratoconjunctivitis was produced in rabbits by exposure to a mercury vapor arc. After the establishment of doses that would result in reproducible signs, alternate eyes were treated by means of a therapeutic heat lamp. No evidence was obtained to indicate that this form of treatment benefited the keratoconjunctivitis."

W ZENTMAYER

PARENCHYMATOUS KERATITIS IN A CASE OF ACQUIRED SYPHILIS TARIK OZERENGİN, Goz klin 1: 52, 1943

The author describes a case of parenchymatous keratitis withritis in a woman aged 40 with syphilis who was observed over a period of seven years. The author concludes that keratitis with gumma of the legs existed and that, contrary to the general belief, the corneal disease may occur not only as a secondary, but as a tertiary, lesion. Treatment with mercury and arsenic brought about rapid improvement, but not without further relapses.

W ZENTMAYER

General

VITAMIN P IN OPHTHALMOLOGY W R MATHEWSON, Brit J Ophth 28: 336 (July) 1944

In 2 cases of ocular hemorrhage vitamin P was used, with satisfactory results. In the first case the patient had extensive retinal hemorrhages and hemorrhages of the nose and bladder, but on administration of vitamin P the nasal and vesical hemorrhages ceased, no fresh retinal hemorrhages occurred and those present were absorbed. The

patient had myelomas and the nasal hemorrhage was characterized by large clots of blood and serum.

In the second case the patient had recurrent hemorrhage into the anterior chamber after extraction of a cataract, but after administration of vitamin P there was no recurrence and the iris, which had become muddy rapidly cleared. The eye which was looking unhealthy rapidly took on a healthy tone. The patient improved greatly and rapidly in general appearance and mental agility when vitamin P was given.

In conclusion it is suggested that there is a case calling for investigation of vitamin P because so far as can be judged from the evidence in these 2 cases, vitamin P is of value in ophthalmology.

W. ZIMMERMANN

General Diseases

MIKULICZ DISEASE [HYPERSTROPHY OF THE SALIVARY AND LACRIMAL GLANDS] M. VILLANUEVA and C. S. DAMEL, Arch de oftal de Buenos Aires 18: 559 (Nov.) 1943.

The author reports a typical case of the disease in a man aged 33. The patient had a history of a primary syphilitic lesion and a positive Wassermann reaction of the blood to which he had received treatment.

The sublingual and parotid glands on the left side were enlarged and tender. The left eye showed some protrusion of the globe, edema of the lids and congestion of the conjunctiva. Treatment was with calcium iodine arsenic, anti-syphilitic drugs and roentgen ray therapy, with no encouraging results.

A brief discussion of the syndrome is given. Photographs of the patient appear in the article.

H. F. CARRASQUILLO

Glaucoma

THE USE OF DORYL [CARBAMINOYLCHOLINE CHLORIDE] IN GLAUCOMA J. F. HARDESTY, Am J Ophth 27: 625 (June) 1944.

Hardesty concludes that carbaminoylcholine chloride is not effective in all cases of glaucoma, and is even contraindicated in some instances, but that from his experience in other cases, as well as in the 9 cited, the drug is a valuable adjuvant in the treatment of glaucoma.

W. S. REESE

SURGICAL CONTROL OF GLAUCOMA IN THE NEGRO C. E. ILIFF, Am J Ophth 27: 731 (July) 1944.

Iliff reaches the following conclusions:

"1 Primary glaucoma in the Negro was controlled in 54.2 per cent of the cases by the filtering operation."

"Secondary glaucoma was controlled in only 44 per cent of the cases by the filtering operation."

"2 Iridencleisis is superior to tiephning as an initial operative procedure and the complications are less severe."

"3 Tiephning or cyclodialysis is the operation of choice as a second operative procedure after one operative failure."

"4 When operative failure occurred, it was noted within the first six months in over 85 per cent of the cases."

"5 Postoperative beta irradiation of the blebs in filtering operations give encouraging results and is worthy of further trial."

W. S. REESE

Hygiene, Sociology, Education and History

VISUAL PHYSIOLOGY OF THE CINEMA GEORGE H. BELL, Brit M J 2: 669 (Nov 27) 1943.

At the Tenement Institute of Ophthalmology, Western Infirmary, Glasgow, Scotland, Dr. George H. Bell from the Institute of Physiology, of the University of Glasgow delivered a lecture on the subject indicated in the title. He anticipates a great exploitation of the moving picture as a teaching medium and therefore thinks it important that medical people should have some elementary knowledge of the physiologic problems concerned with moving pictures. For educational purposes, a 16 mm equipment is regarded as satisfactory. The details of the picture can be clearly seen if the observer is seated not more than 6 screen widths from the screen. Those who are seated nearer find that the picture lacks sharpness and that the accommodation is apt to tire, and they experience flicker and other symptoms of fatigue. The screen with the usual 2 inch (5 cm) lens should be 5½ screen widths from the screen. The best position to get a perspective of the projected pictures is halfway back. It is also important not to sit too much to the side. For school projection the viewing angle should not be more than 30 degrees. The committee recommended (a) that a picture width equal to one-sixth the distance from the farthest row of seats to the screen position should be adopted for classroom projection, (b) that no pupil should be seated closer to the screen than twice the picture width and (c) that no row of seats should be longer than its distance from the screen. The screen with a mat surface is 90 per cent as bright at an angle of 30 degrees as when viewed directly from the front, while a screen coated with small glass beads is four times as bright, but the maximum viewing angle is narrowed to 20 degrees. For a square room the mat screen is the best, and the coated type may be used in a long room. The brightness of the projected picture should be 10 foot lamberts with the projector running, but with no film in the machine. The efficiency is lost if the light is

too weak or if it is too strong. The quality of the picture suffers, also, if the projection room is not adequately darkened.

The author concludes with comments on the illusion of reality and states that even when stereoscopy is added, many things will still be missing for complete illusion.

ARNOLD KNAPP

Ocular Muscles

OPHTHALMOPLEGIA AND RETINAL DEGENERATION R I BARNARD and R O SCHOLZ, Am J Ophth 27 621 (June) 1944

Barnard and Scholz give the following summary:

"Four cases of various types of retinal degeneration with complicating ophthalmoplegia are reported. Although other factors were present which might account for the ophthalmoplegia, it was felt that the association is more than a coincidence. It is suggested that the two constant features in these cases, ophthalmoplegia and retinal degeneration, with secondary pigmentary changes may be a syndrome due to some common etiologic factor."

W S REESE

CORRECTION OF EXTERNAL-RECTUS PARALYSIS WITH CONTRACTURE OF THE OPPOSING INTERNUS P H REINHARDT, Am J Ophth 27 636 (June) 1944

Reinhardt states that transplantation operations often a cosmetic and functional cure for paralyses of the external rectus muscle which do not clear up and that operation should be performed before contracture of the internal rectus muscle occurs.

W S REESE

Parasites

ORBITAL MYIASIS L A BARRIERE, Arch de oftal de Buenos Aires 18 585 (Nov) 1943

The author discusses the rare condition of ophthalmomyiasis and reports a case in which it involved the orbit. The disease was present in an inmate of an insane asylum. An extensive ulceration took place in the right orbit, which destroyed the lower lid and extended almost to the apex of the orbit. The first two phalanges of the index and middle fingers could be placed in the opening. Larvae were encountered at the base of the ulceration in great numbers. According to the parasitologic report these larvae belonged to the genus Chrysomyia, species Cochliomyia hominivorax the fly which produces myiasis in animals. Owing to the extension of the ulcerative process, the eyeball was wholly destroyed. The condition was treated by removal of the larvae (153 of which were found) and daily intravenous injections of mercuric oxycyanide. The patient was cured.

H F CARRASQUILLO

Physiology

THE SECRETION-DIFFUSION THEORY OF INTRACULAR FLUID DYNAMICS V E KINSEY and W M GRANT, Brit J Ophth 28 355 (July) 1944

From comments on the authors' recent article (The Mechanism of Aqueous Humour Formation Inferred from Chemical Studies on Blood-Aqueous Humour Dynamics, *J Gen Physiol* 26: 131 [Nov] 1942) Kinsey and Grant feel that recapitulation of their theory of intraocular dynamics is in order. They summarize their present concept of aqueous humor dynamics by stating their belief that the electrolytes enter the anterior chamber as a result of secretion and the nonelectrolytes by diffusion. Both electrolytes and nonelectrolytes, they believe, leave the anterior chamber by a process of flow. The authors then discuss the criticism made by Duke-Elder and Davson of their statement of the mechanism of ultrafiltration and outflow.

W ZENTMAYER

Retina and Optic Nerve

A TYPE OF FOVEO-MACULAR RETINITIS OBSERVED IN THE U S NAVY F C CORDES, Am J Ophth 27 803 (Aug) 1944

Cordes describes an unusual type of foveomacular retinitis seen in Navy personnel in the Hawaiian and South Pacific areas. The lesion is limited primarily to the fovea and starts with macular edema. Later the picture is that of a hole or cyst in the fovea surrounded by a gray area. This may eventuate in a honeycombed condition. Treatment seems ineffective, and the etiologic agent has not been determined.

W S REESE

ALMOST COMPLETE RETINAL DETACHMENT AFTER CATARACT EXTRACTION, COMPLETE REATTACHMENT AFTER GLAUCOMA ATTACK F NELSON, Am J Ophth 27 876 (Aug) 1944

Nelson reports a case of total detachment of the retina in a man aged 80 following intracapsular extraction of a hypermature cataract. The detachment persisted for several months, during which the eye was practically blind. Complete reattachment and full restoration of function then occurred, after an acute glaucomatous attack.

W S REESE

EMBOLISM OF A BRANCH OF THE CENTRAL ARTERY OF THE RETINA WITH CURE REPORT OF TWO CASES P SATANOWSKY, Arch de oftal de Buenos Aires 18 579 (Nov) 1943

Alterations in the endothelium of the left side of the heart or the aorta may produce a coagu-

lum which may give rise to an embolus. The walls of the artery at the level in which the embolus is lodged react and embolic arteritis results. The changes in the territory supplied by the vessel depend on the terminal character of the artery or the existence of insufficient anastomotic branches. When the embolus is small and has been retained by a reactive spasm of the vessel, it may migrate to a smaller branch on relaxation of the spasm through treatment the visual disturbances may then be much reduced or may disappear altogether if the embolus is washed out by the blood current.

The author describes 2 cases in which such results were obtained after treatment with the antispasmodic drugs acetylcholine and meotinic acid.

J. F. CARRASQUILLO

Toxic Amblyopia

THE ETIOLOGY AND TREATMENT OF TOBACCO-ALCOHOL AMBLYOPIA F. D. CARROLL Am J Ophth 27: 712 (July) 847 (Aug.) 1944

Carroll gives this summary and draws the following conclusions:

"Approximately 175 patients with tobacco-alcohol amblyopia have been observed by the writer in the nine-year period 1933-1942. In the last seven years 25 of these patients have been allowed to maintain their usual intake of alcohol and tobacco under the following conditions:

"An initial group of 11 patients was placed on a diet adequate in all respects and supplemented with brewers' yeast.

"A second group of five patients was left on its usual diet and given vitamin-B complex.

"A third group of four hospitalized patients was placed on a diet inadequate in all known vitamins and given large amounts of vitamin-B complex.

"A fourth group of five hospitalized patients was placed on the same inadequate diet and given synthetic vitamin B₁ only.

"All the patients on these various regimes made partial or complete recoveries in spite of

then continued and unabated use of alcohol and/or tobacco. The vision in 21 patients was 20/30 O.U. or better after treatment and in 14 was 20/20 or better. These results were at least as good as those obtained by the author in any previous consecutive 25 patients with this condition, including those who abstained from the use of tobacco and alcohol while under treatment.

"The fact that all of the patients in the fourth group improved and one made a complete recovery is of special significance since in this group every known factor other than vitamin B₁, which might have caused improvement had been eliminated. In spite of this result, however, it is recommended that the whole vitamin-B complex be administered as well as thiamin alone in the treatment of these cases."

The most likely explanation of tobacco amblyopia at this time is that it is the result of a "toxic" action of tobacco on malnourished cells. When thiamine is added, the nutrition of the damaged cells or perhaps their axons, improves and the injurious agent is no longer injurious. It seems likely from present evidence that in persons consuming absorbing and utilizing normal amounts of vitamin B tobacco amblyopia does not develop.

W. ZENTMYER

CORRECTIONS

In the article by Dr. Carlos Weskamp entitled "Bowen's Disease of the Cornea," in the April issue (ARCH. OPHTH. 31: 310, 1944), "osteitis deformans" was erroneously inserted in line 3 of the fourth paragraph. The term Paget's disease refers here to the cutaneous disease of the nipple.

In the abstract of a paper by Dr. William F. Hughes entitled "Chemical Burns of the Eye," in the November 1944 issue of the ARCHIVES, "or a 0.05 molar solution" on line 9 of the paragraph on "Alkali Burns," should read "and a 0.05 molal solution."

Society Transactions

EDITED BY DR W L BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION ON OPHTHALMOLOGY

FRANK C KEIL M D *Chairman*

WILLIS S KNIGHTON, M D *Secretary*

May 15, 1944

End Results of Intraocular Foreign Bodies

DR FREDERICK H HULL, Passed Assistant Surgeon, United States Public Health Service (by invitation)

The end results obtained in any given case of intraocular foreign body depend largely on the amount of damage done to the structures of the eye as the foreign body travels through the globe. Hemorrhage in the vitreous of any extent is usually serious, and the development of infection, particularly panophthalmitis, is disastrous.

At the Marine hospital with which I am associated the practice is to attempt removal with the hand magnet through the wound of entrance, with the use of local anesthesia and retrobulbar injection of procaine, when the foreign body is in the iris or the anterior chamber. The corneal wound is then covered with a conjunctival flap. If the wound of entrance has healed, the foreign body is removed through a keratome incision.

When the foreign body has been localized in the vitreous chamber, my associates and I have employed both the anterior and the posterior route. With the first approach, the giant of the hand magnet is used to bring the foreign body to the posterior capsule of the lens, through the zonule and then into the anterior chamber, from whence it can be removed through a keratome opening. When removal is attempted by the posterior route, the scleral site nearest the foreign body is laid bare and the foreign body removed by means of the hand magnet through a radial sclerotomy opening. Diathermy punctures are placed routinely about the scleral incision. The posterior approach has given better results than the anterior approach. All patients receive either a prophylactic dose of tetanus antitoxin or a "booster dose" of tetanus toxoid. Oral administration of sulfathiazole and sulfadiazine has not seemed to lessen the incidence of infection.

In a series of 24 consecutive cases encountered prior to 1943, the foreign body was in the anterior chamber in 37 per cent and in the posterior chamber in 63 per cent. Of the cases in which the body was in the anterior chamber, good vision was retained in 55 per cent; cataract developed in 22 per cent and

enucleation was necessary in 11 per cent. Of the cases in which the foreign body occurred in the posterior chamber, useful vision was retained in only 27 per cent; cataract developed in 27 per cent, a hemorrhage in the vitreous large enough to cause serious visual loss occurred in 13 per cent, and the process went on to enucleation in 33 per cent.

The following cases are reported as clinical examples of some of the results obtained, both good and bad.

REPORT OF CASES

CASE 1—A carpenter's mate aged 26 felt something hit his left eye while clawing a nail from a piece of wood. The next day vision was 14/21 in the right eye and 14/89 in the left eye. There was a laceration of the cornea 2 mm long at 9 o'clock on the limbus. A metallic foreign body beneath this impinged on the iris at 10 o'clock. The foreign body was removed with the hand magnet through the wound of entrance on the day of examination. Convalescence was uneventful except for a moderate amount of iritis. The tension has remained normal for two months, and vision is 20/20 —1 m each eye.

CASE 2—A machinist aged 45 put his glasses on his forehead, and a chip from the hammer of a fellow-worker, 3 or 4 feet (90 or 120 cm) away, struck his right eye, producing a penetrating wound of the cornea directly below the pupil. The anterior chamber was cloudy and the iris was pulled downward. Roentgenographic examination revealed a foreign body 8 by 2 by 1.5 mm, situated in the vitreous chamber. With the hand magnet the foreign body was extracted through the wound of entrance. The progress was steadily downhill. The lens became cataractous. The eye was severely inflamed, and vision was completely lost. The tension was below normal. Two months later the right eye was enucleated, with the patient under anesthesia induced by intravenous injection of sodium pentothal. Convalescence from this operation was uneventful.

CASE 3—A shipfitter aged 49 felt something hit his left eye when drillers drilled through from the other side of a bulkhead on which he was hammering. Vision was 20/30 in the right eye and was limited to hand movements in the left eye. A penetrating wound of the sclera, 2 mm long, lay 3 mm behind the limbus, at 4 o'clock. The cornea, the anterior chamber and the lens were clear, but the vitreous was filled with blood. Roentgenographic examination and localization by the Sweet method revealed an intraocular foreign body, 2.5 by 2 by 2 mm, situated 10 mm below the horizontal plane, 2 mm nasal to the vertical plane and 7 mm behind the cornea. Operation was performed on the day of admission, the hand magnet being used to bring the foreign body through the zonule and into the anterior chamber, from which it was removed through a keratome incision. The foreign body on withdrawal became enmeshed in the iris, a small portion of which prolapsed. This portion was excised. The keratome section healed normally, but the scleral wound did not close completely, so a conjunctival flap was placed

over the wound. Subsequently the scleral wound healed normally. Six weeks after the accident a traumatic cataract began to develop. The tension has remained normal for seven months but the cataract has become increasingly dense. Vision was 20/20 with correction in the right eye and was limited to light perception in the left eye.

CASE 4—A laborer aged 38 felt something hit his right eye while cutting a piece of tin with a hammer and chisel. He was treated at another hospital for two weeks before I saw him.

At that time vision was corrected to 20/20 in each eye. No wound of entrance was noted in the cornea or the sclera. The vitreous was fluid, and a few floaters were present. Roentgenographic localization by the Sweet method revealed a foreign body 6 mm below the horizontal plane 5 mm temporal to the vertical plane and 16 mm behind the cornea. One week later the foreign body was withdrawn posteriorly by the hand magnet through an L-shaped scleral incision. Diathermy punctures were placed about the sclerotomy opening, and the conjunctiva was closed. Convalescence was uneventful. Vision in each eye remained 20/20 with correction.

Four years after the accident the patient complained of blurred vision in the right eye. There was no pain. No previous attacks had been noted. Vision was corrected to 20/25 in each eye. The cornea of the right eye was hazy. The disk was indistinct, but no increased cupping was seen. Tension was 60 mm (Schiotz) in the right eye and was normal in the left eye. The patient was confined to bed, and 1 drop of a 1 per cent solution of pilocarpine nitrate was instilled every two hours in the right eye. The tension decreased promptly to normal and has remained so. He has returned for observation every two months since that time, and the fields and fundi remain normal.

DISCUSSION

DR CONRAD BERENS Dr Hull's report is most interesting to me, especially because of his preference for the posterior route in the extraction of many intraocular foreign bodies. Although I was originally trained to remove most intraocular foreign bodies by the anterior route after first drawing them into the anterior chamber with the magnet, I have recently removed more such foreign bodies posteriorly.

I like to ring the incision with electrolytic punctures. Because some foreign bodies which were originally considered nonmagnetic proved to be magnetic after enucleation, and because my associates and I have apparently had success in similar cases with use of the Berman localizer, I am convinced that in all cases of doubt this added means of accurate localization of foreign bodies should be employed. We have so far used this instrument in 10 cases at the New York Eye and Ear Infirmary, and in 4 cases we believe the localizer has been of material assistance in the operation.

Even though the roentgenologic localizing method and the Comberg technic with the contact glass are excellent, more exact localization is sometimes desirable when a foreign body is enmeshed in the tissue.

Paralysis of the Superior Rectus Muscle, Exophthalmos, Pseudoptosis and Fibrosis of Inferior Rectus Muscle Following General Anesthesia DR CONRAD BERENS and CAPTAIN GERALD FONDA, Medical Corps, Army of the United States

This article will be published in full, with discussion, in a future issue of the ARCHIVES.

Evaluation of Results in a Series of Corneal Transplants DR R TOWNLEY PATON

The operation for the removal of corneal scars has now well stood the test of time. No longer may one doubt the permanence of improvement in sight obtainable by corneal transplantation in carefully selected cases. Corneal surgery has met all the vicissitudes and platitudes to which in the past cataract surgery was subjected. Let the young ophthalmic surgeon be taught that this operation is simple, easy to perform and often successful in restoring sight.

The various technics are easily acquired. Although every surgeon is likely to modify the operation in one way or another, certain principles must be strictly adhered to.

1 The donor's graft must be traced and carefully dissected. Whether a square or round graft or one of some other shape is used makes little difference except from the cosmetic point of view, so long as the edges are even and smooth.

2 An exact tracing (never smaller than the donor's graft) on the recipient's cornea and an equally careful dissection are essential, special care being given of course to the internal structures of the eye, the iris, lens etc.

3 Beveling should be avoided as much as possible, in either the donor's or the recipient's eye as it only leads to an imperfect fit.

4 Sutures should be inserted before the anterior chamber is penetrated. The sutures should be placed as close to the traced edges as possible.

5 Two sutures are preferable to one because they are easier to tighten, more even distribution of pressure is obtainable, especially when there is a tendency to overriding of one edge of the graft, and there is less danger of complication if one suture is accidentally cut.

6 Use of conjunctival flaps invariably leads to complications and should be discouraged.

7 The donor's eye should be carefully selected, and young eyes are probably better than old eyes. Until corneas are obtainable in large quantities, it has been the tendency to use only healthy-appearing corneas, regardless of race, blood group or age.

8 As yet little is known about the problem of corneal vascularization and its prevention. Roentgen ray therapy, given a day or two after

operation, has been tried, but my experience is limited to only a few cases.

Postoperative care of the graft offers one of the greatest avenues for research in the future.

In a limited experience of 50 cases carefully studied at the Manhattan Eye and Ear Hospital, and another 50 cases studied in Baltimore and at the Flower-Fifth Avenue Hospital several years ago, my results are encouraging. In nearly all cases sight was improved. In 3 cases the eyes were lost. In 4 cases serious post-operative conjunctivitis developed, which spoiled what might have been an excellent result. In only 2 cases was vision of 20/30 obtainable—improvement in 1 case being from 10/200 and in the other from 20/200. The average improvement was from ability to count fingers at 2 feet (60 cm.) to visual acuity of 20/200.

One patient had a particularly successful graft done on one eye, vision improving from perception of hand movements to 20/50. At the end of three years the graft is beginning to cloud over. The other eye has had four grafting operations, a cataract extraction and a trephination; this eye is now ready for a fifth operation, as the tension is down and vision as good as when treatment was started, several years ago.

DISCUSSION

DR RAMÓN CASTROVIEJO As Dr Paton said, keratoplasty is an operation with which all ophthalmologists should become acquainted because, although it requires a high degree of accuracy, it can be performed by any one who has been well trained in ophthalmology. At the Institute of Ophthalmology of the Columbia-Presbyterian Medical Center, the residents perform keratoplasties with results comparable to those obtained by men who have had more experience in this type of surgery.

In properly selected cases excellent visual improvement may be expected. In favorable cases the average vision obtained is generally better than 20/50. It is not infrequent to obtain vision of 20/20. In some of the cases in which operation has been performed at this institute vision of 20/15 has been obtained. Some of the patients operated on for corneal transplantation have been able to engage in occupations requiring a great deal of use of the eyes, such as bookkeeping; other men with corneal transplants have been inducted into the armed forces, with normal vision.

Dr Paton mentioned keratoplasty for cosmetic purposes. It has been the experience of my associates and myself that in a small percentage of cases, perhaps in no more than 1 per cent, is corneal transplantation needed for cosmetic purposes. For such purposes Dr Paton prefers the round transplant. I prefer the square one for I feel that it is easier to graft. If the transplant remains clear the shape of the graft can be seen with difficulty because the scars are almost

invisible a few months after the operation. On the other hand, if the transplant becomes opaque, the shape of the graft does not matter because it looks bad anyway.

I agree with Dr Paton in regard to beveling. In my opinion beveling of the donor's graft is not necessary, but I believe it is desirable to have a slight beveling of the endothelium of the host's cornea in order to counteract the tendency of the endothelium to roll inward and thus leave a gap in the posterior surface which will become filled with fibrin. The conditions for adhesion of the iris to this gap are favorable if the pupil is not fully dilated. The slight beveling of the endothelium brings about a better approximation of the posterior layers of the graft and the cornea of the host, so that early restoration of the anterior chamber is facilitated and formation of anterior synechias and subsequent nebulosity of the graft, and in some cases secondary glaucoma prevented.

Contrary to what Dr Paton has stated namely, that two sutures are better than one to hold the graft in position because they make a more uniform pressure, it has been my experience when I used two sutures that one of them might press on the transplant more than the other and thus interfere with the even cicatrization of the graft. This unevenness of pressure is prevented by use of a continuous suture.

At the Institute of Ophthalmology corneas taken from Negroes have been used in keratoplasties on white patients, and vice versa. The results have been similar to the results in cases in which white patients and Negroes had transplants of donor material obtained from persons of their own race. The work of Elschner, Filatov, Thomas and myself has shown that the blood group has no bearing on the success or the failure of keratoplasty.

Dr Paton mentioned the use of roentgen radiation two or three days after the operation to prevent vascularization of the graft. In my experience I have not noticed vascularization of the graft until the third or fourth week after corneal transplantation. If roentgen radiation is to be employed to prevent vascularization of the graft, it should be begun no sooner than two weeks after the operation. To use roentgen radiation only two or three days after operation encourages the formation of anterior synechias with subsequent opacity of the graft and possibly secondary glaucoma.

In the case Dr Paton reported in which a corneal transplantation had been performed on a cornea with calcareous degeneration, probably more benefit would have been derived from a superficial keratectomy than from a corneal transplantation. Similar cases in our hands resulted in failure when a corneal transplantation was performed, and in a high percentage of cases successful results were obtained after superficial keratectomy.

The problem of corneal transplantation cannot be discussed in a few minutes. There are many points that would require extensive discussion, such as the indications for keratoplasty. The indications for this type of operation are definite, at the Institute of Ophthalmology my associates and I have been able to tell with an accuracy of almost 99 per cent which cases are favorable for corneal transplantation and which are not. It has also been possible to foretell the cases in which a high percentage of transparent grafts were likely to result and those in which the transplant would become nebulous or opaque. Once the indications for keratoplasty have been well established it would be as useless to operate in a case in which no hope of improvement of vision was offered as it would to operate in a case for cataract when the perception and projection of light are defective.

It is regrettable that the lay publications have dramatized this subject so extensively, stimulating false hopes among the public, who expect this operation to be effective with all kinds of conditions and who, the more it is publicized, will hope for miracles, no matter how accurately the indications for this type of treatment are explained to them.

By now the possibility of dramatization of this problem has almost exhausted itself, and in the future it is to be hoped that members of the medical profession will be left alone to work without interference for the benefit of all.

DR CONRAD BERENS I am deeply interested in this splendid presentation, as I am sure all have been, but I am disturbed by the number of patients who come with false hopes of obtaining cure for blindness. How many patients considered sufficiently blind to be institutionalized, or needing guidance by a Seeing Eye dog, have been benefited by corneal transplantation to a point at which they were able to engage in occupations for which good vision is usually needed? Might not these same patients have been equally benefited by optical iridectomy or superficial keratectomy?

My experience with the New York Association for the Blind and a home for blind babies as well as my long association with the work of the American Foundation for the Blind and the National Society for the Prevention of Blindness, makes me believe that the answer to this question is important. I have yet to see a single patient in the category of the blind who was benefited by a corneal transplant and could not have been helped almost as much by optical iridectomy or keratectomy. Certainly, the statement that 100,000 patients in the United States could be made to see through this operation is a bit fantastic, and I am glad that Dr Paton stressed that too much had been made of this problem in the newspapers and in other publications.

This leads to the case of calcareous deposits which Dr Castroviejo mentioned. I asked Dr Paton whether he had here a section of the cornea, for it is my impression that most of these calcareous deposits are superficial, and I have had good results with superficial keratectomy in cases of this condition.

I agree with Dr Paton on the question of sutures, for I have been interested in the use of two sutures instead of one, one white and the other black the two being locked in the episcleral tissue with a small strip of plastic material. With this technic I believe I can equalize the tension more satisfactorily, and the manipulation of the sutures is much simpler.

I should like to know Dr Castroviejo's technic for making a square incision, that is, how he obtains an approximately straight upper edge where the keratome is introduced.

DR R. TOWNLEY PATON I agree with Dr Berens about the number of people who are actually blind and can be helped by this operation.

With regard to Dr Castroviejo's point I feel that a round window more closely resembles the pupil and that as the opacity of the cornea extends well beyond the central area in a majority of cases, trephination should be used wherever possible. This holds true particularly for women.

With regard to cutting the edges, I cannot state definitely that some beveling is not obtained, but I certainly do not try to bevel after I have once punctured the anterior chamber. It might be well always to use a cataract knife to puncture the anterior chamber, because the ordinary keratome and the Agnew knife are angled in such a way that it is almost impossible to make a right-angled puncture into the anterior chamber. I have used a modified keratome with satisfactory results.

DR RAMÓN CASTROVIEJO In answer to Dr Berens, the keratome should be used only to make an opening into the anterior chamber through which one of the blades of the scissors is introduced in order to complete the corneal incision. No attempt should be made to cut down with the keratome perpendicular to the cornea because in this position the keratome may injure the lens. Of course, this does not apply to the case of the donor, as it does not matter whether his lens is injured.

Traumatic Subconjunctival Dislocation of the Lens. Report of a Case DR DONALD WEEKS BOGART

The patient was seen five days after an automobile accident in which the pelvis and the occipital bone were fractured. Vision in the right eye was reduced to perception of light. There was a cystic mass the size of a pea under the unlacerated portion of the conjunctiva just anterior to the insertion of the superior rectus

muscle The iris was drawn up, the appearance suggesting an operative wound. With ultraviolet light the mass was fluorescent, proving that it was the lens.

The lens was easily removed through the conjunctival incision, the iris was excised where it was prolapsed, and the sclera was closed. The postoperative course was uneventful, and on the patient's discharge, a month later vision had improved to perception of hand movements, although the vitreous had not yet cleared of hemorrhage resulting from the accident.

The causes of lenticular dislocation of this type are discussed. The reasons for presentation of this case are as follows: (1) the interesting nature of the diagnostic problem and the arrival at the diagnosis on the basis of examination with ultraviolet light, (2) the speedy recovery following removal of the lens, absorption of which would have taken considerable time and (3) the necessity for closure of the sclera and of inspection of the ciliary body.

Binocular Papilledema in a Case of Torulosis (Pathogenic Yeast Infection) Associated with Hodgkin's Disease DR MARTIN COHEN

This paper was published in full in the December issue of the ARCHIVES, page 477.

Meningioma of the Sphenoidal Ridge Report of a Case DR RUDOLF AEBLI

A 7 year old boy had a history of gradual protrusion of the left eye, of one year's duration. The eye was pushed down and in, and abduction and elevation were limited. Vision was 20/20 in each eye, and examination of the fundus revealed nothing significant. Roentgenograms taken at various intervals ultimately showed bony changes in the left sphenoid ridge and around the left superior sphenoid fissure. The diagnosis was neoplasm of the middle fossa with extension into the orbit. A left frontoparietal craniotomy, performed by Dr. Joseph King in July 1939, revealed a firm mass, the size of a silver dollar, adherent to the dura over the area of the left sphenoid ridge. In November 1939 a left temporal transconjunctival approach to the ethmoid-orbital area was made, and two globular masses, one measuring 2 cm and the other 3 cm in diameter, were removed. Adhesions to the lids were produced. Examination of tissue showed that both the orbital masses and the intracranial mass had the characteristic structure of a meningioma.

In November 1940 the boy was readmitted to the hospital with an increase in the exophthalmos, papillitis and progressive loss of vision. Roentgenograms showed dense bony shadows in the sphenoid ridge, the roof of the orbit and the lateral walls and floor of the orbit. A second frontoparietal craniotomy was performed by Dr.

Joseph King, and the sphenoid ridge and the roof and lateral wall of the orbit were removed. In January 1942 the left orbit was exenterated. The latest roentgenograms showed dense bony shadows in the maxillary area and in the malar bone on the left side. The patient has now been followed for six years, and, except for the local symptoms and signs about the left orbit, the boy is well.

In cases of slowly progressive unilateral exophthalmos with limitation of abduction and elevation, frequent stereoscopic roentgenograms of the orbit should be taken. An early intracranial approach is essential, for once the tumor has invaded the bone and extensive bony infiltration is present, it is impossible to remove the osteoma completely.

DISCUSSION

DR JOSEPH E J KING This is the youngest person on whom I have ever operated for the meningioma of the sphenoid ridge. The tumor usually occurs in older people. This tumor invaded the bone and thickened it greatly. At the time Dr. Aebl and I first saw the boy we did not know the details in the case and removed the roof of the orbit and the frontal ridge, as advised by Dr. Gilbert Horrax. If I am not mistaken, this tumor also invaded the orbit, forming a dumbbell-shaped mass. The tumor involving the bone extended slowly, as Dr. Aebl described, entered the base of the wing of the sphenoid bone and extended into the left malar bone, and possibly backward into the bones forming the base of the skull. After exenteration of all the contents of the orbit, we later removed the left malar bone and completely uncovered the antrum, covered it with cutaneous flaps and inserted a drain in the antrum. Shortly after this procedure an opening was made into the inner wall of the antrum through the nose to provide drainage. When the contents of the orbit were completely removed and the optic nerve was divided near its entrance to the orbit, there followed a considerable flow of cerebrospinal fluid, and we feared infection of the meninges might occur. The amount of fluid which escaped in a day was enormous, the fluid wetting the dressing thoroughly and running down the patient's cheek. We filled the orbit partly with a sulfonamide powder and packed it with gauze, and slowly and gradually the leakage ceased, without development of meningitis. One of our colleagues remarked that we were wasting time on this boy, but the child has lived for several years, and he is still getting along well. I think that after all the expenditure of time was worth while.

DR JAMES W SMITH The report of Dr. Aebl is a reminder that meningioma must be fairly common. Ten years ago Dr. Cohen reported a case before this section, Dr. Knapp reported 2 cases before the American Ophthalmological Society in 1938, and Dr. Kirby pre-

sented 1 case in discussion, I presented a case before this society in 1939 and Dr Givner has 2 cases under observation in which the diagnosis has been verified roentgenographically. Roentgenography is invaluable, and yet a flat roentgenogram made in my case and in Dr Knapp's first case failed to establish the diagnosis. A clinical fact worth mentioning is that stereoscopic roentgenograms are essential for accurate localization.

Dr Aebli did not mention the diagnostic point with regard to suprazygomatic swelling which I emphasized in my paper (*Meningioma Producing Unilateral Exophthalmos*, Arch Ophth 22:540 [Oct] 1939). The swelling was evident in the photograph of his patient, it is a valuable clinical sign of earlier appearance than the exophthalmos which as Dr Aebli stressed, was slowly progressive painless nonpulsating and unilateral.

As Dr King stated most meningiomas of the sphenoid ridge occur in middle-aged patients and the extensive involvement observed in this child was unusual. I had the good fortune to communicate with the late Dr Harvey Cushing, who was the pioneer in meningioma research. He stressed that in most of his cases the tumor occurred in females and on the left side. He also observed in his series of cases of meningioma that most of the women had the suprazygomatic fulness but dressed them hair over the swelling in such a manner that the clinician missed an important diagnostic sign. I profited by Dr Cushing's comment and had the photograph of my patient taken with her hair combed up and tied with a ribbon.

It is almost impossible for a neurosurgeon to remove all the area of hyperostosis. In my case about seven eighths of the tumor was removed, and the exophthalmos receded 2 mm. During the past year the exophthalmos has slowly recurred, but vision is normal. I plan to do a tarsoorrhaphy to narrow the width of the palpebral fissure as the advanced age of my patient would preclude another major neurosurgical operation.

DR ALFRED KESTENBAUM: All should be grateful to Dr Aebli for his drawing attention to this important condition. Sometimes the ophthalmologist is able to arrive at the diagnosis early. In May 1942 I saw a woman approximately 56 years of age with slight exophthalmos of the left eye, of only 1 mm. There was slight paresis of the left superior rectus muscle, motility in upward gaze was only 1 mm less than that of the other eye, but the diplopia was significant. For a white object there was a relative central scotoma, which extended downward. For a red object the entire lower half of the field, including the center, was defective. Vision was reduced to 20/100. The temporal part of the disk was slightly pale. All these signs pointed to the diagnosis of a retiobulbar space-taking

process, apparently in the posterior upper part of the orbit. I made a tentative diagnosis of meningioma of the left sphenoid ridge. One month later exact measurement revealed slight but definite deterioration in every aspect. The exophthalmos was 2.5 mm., the elevation of the left eye was a little more restricted (defect about 2 mm.). In addition, there was slight ptosis, vision was slightly less than before, and the scotoma was increased. I made a diagnosis of progression of the meningioma and advised operation. Permission, however, was refused, and I saw the patient three months later, in September. Visual acuity was now reduced to ability to count fingers at 1.5 meters. The scotoma for white objects was absolute. The elevation of the eye was still more restricted and the degree of exophthalmos a little increased. An exploratory operation, by Dr Leo Davidoff, revealed a meningioma of the left sphenoid ridge, and this was removed. After operation the exophthalmos was less pronounced, but vision remained unchanged. It is not yet two years since the operation, so that a definite prognosis cannot be given, but up to the present, aside from the decreased vision, the patient is well.

DR RUDOLF AEBLI: Dr Smith, the roentgenograms were stereoscopic, and taken by Dr F M Law.

With regard to the question whether the fulness over the left zygoma is an early sign, I suspect that by the time fulness appears the meningioma will already have invaded the retiobulbar area or the temporal fossa. I do not see how fulness here could be an early sign, for it must be due to edema or swelling, but it is a definite sign.

Metastatic Orbital Tumor with Exophthalmos: Report of a Case DR DONALD BALL

A white man aged 70 complained of protusion of the left eye with diminution of vision, of only one week's duration. His health had been good until two months prior to admission to the hospital, when he noted occasional expectoration of blood-stained sputum, there was loss of weight of 20 pounds (9.1 Kg) in the month before admission, and for three weeks prior to entrance to the hospital there had been slight swelling of and pain in the left cheek.

Visual acuity was 20/40 in the right eye and 3/200 in the left eye. There was pronounced proptosis of the left eye, with limitation of motion in all directions. The corneal apex pointed downward. A fulness was felt below the globe and inside the orbital rim. The globe was tender, and the tension was high. The pupil was dilated, and its reactions were sluggish. The fundus showed dilated and tortuous veins and early papilledema. There was notable constriction of the visual field. The right eye was normal.

The patient was extremely emaciated. The final clinical diagnosis was bronchogenic carcinoma with metastases to the left orbital area and to the brain.

Twelve days after admission removal by aspiration of a specimen for biopsy from the inferior temporal region of the left orbit revealed a firm mass, about 10 mm in depth, against the posterior wall. A week later, because of the rapid deterioration of the left eye, the contents of the orbit were exenterated. A dense tumor mass was encountered just inside the rim of the orbit. The posterior, inferior and superior walls of the orbit were eroded, and a large amount of tumor tissue remained in the posterior portion of the orbit.

The postoperative course was downhill, and the patient died three weeks later. Autopsy revealed a primary squamous cell carcinoma of the left maxillary sinus, which had invaded through direct extension, the left orbital fossa and, subsequently, the anterior cranial fossa. Metastases were present in the lungs.

This case was thought of sufficient interest for a report because the exophthalmos was unilateral, the cause presented a diagnostic problem, the operation was difficult and the condition was rare.

DISCUSSION

DR DONALD WEEKS BOGART The primary fact which misled Dr Ball and me was the medical report of a lesion in the lung, we concluded that the patient had a primary bronchogenic carcinoma. The specialists in nose and throat disease did not have a chance to look at the antrum. If they had, I am certain that we should have been put on the right track.

During the operation, the bone in the roof of the antrum and the roof of the orbit were observed to be very soft, it is surprising that this condition did not show in the roentgenogram. On careful probing backward we believed that we encountered brain tissue, and autopsy verified this. The tumor had extensively invaded the cerebral cavity and the antrum. I feel that the final diagnosis should not be made without consultation.

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

The National Society for the Prevention of Blindness, Inc.—A prize of \$500 is offered by the National Society for the Prevention of Blindness, Inc., 1790 Broadway, New York 19, for the most valuable original paper adding to existing knowledge about the diagnosis of early glaucoma or the medical treatment of noncongestive glaucoma. This award will take the place of two separate prizes of \$250 each which were announced some time ago.

Papers may be presented by any practicing ophthalmologist in the Western Hemisphere and may be written in English, French, German, Italian, Spanish or Portuguese. Papers written in the last four languages should be accompanied with a summary in English.

Ophthalmologic Seminar, Emory University School of Medicine—An ophthalmologic seminar, sponsored by Emory University School of Medicine, honoring the memory of Dr Abner Wellborn Calhoun, M.D., LL.D., who was born April 16, 1845, will be held in Atlanta, Ga., April 19 to 21, 1945. Dr Calhoun was the first professor of ophthalmology of Emory University and a pioneer in southern ophthalmology. All who are interested in ophthalmology are invited to attend as guests of Emory University.

The guest speakers will be Dr W L Benedict, Dr John Dunnington, Dr Harry Grable, Dr Parker Heath, Dr Walter I Lillie, Colonel Derrick Vail and Dr Frank Walsh.

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Secretary-Treasurer Dr Linley C Happ, 124 Water-
man St, Providence
Place Rhode Island Medical Society, Library, Prov-
idence Time 8 30 p m, second Thursday in
October, December, February and April

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AND OTO-LARYNGOLOGY

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ville
Secretary Dr J H Stokes, 125 W Cheves St
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Secretary Dr M K McCullough, 1717 Pacific Ave
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Lake City
Secretary-Treasurer Dr Charles Ruggeri Jr, 1120
Boston Bldg, Salt Lake City
Place University Club, Salt Lake City Time 7 00
p m, third Monday of each month

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President Dr Mortimer H Williams, 30½ Franklin
Rd S W, Roanoke
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Secretary Dr Welch England, 621½ Market St,
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LOCAL

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Secretary-Treasurer Dr V C Malloy, 2d National
Bank Bldg, Akron, Ohio
Time First Monday in January, March, May and
November

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President Dr B M Cline, 153 Peachtree St N E,
Atlanta, Ga
Acting Secretary Dr A V Hallum, 478 Peachtree
St N E, Atlanta, Ga
Place Grady Hospital Time 6 00 p m, fourth Mon-
day of each month, from October to May

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Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,
Baltimore
Secretary Dr Thomas R O'Rourke, 104 W Madison
St, Baltimore
Place Medical and Chirurgical Faculty, 1211 Cathedral
St Time 8 30 p m, fourth Thursday of each
month from October to March

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President Each member, in alphabetical order
Secretary Dr Luther E Wilson, 919 Woodward Bldg,
Birmingham, Ala
Place Tutwiler Hotel Time 6 30 p m, second
Tuesday of each month, September to May, inclusive

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President Dr Michael J Buonaguro, 589 Lorimer St,
Brooklyn
Secretary-Treasurer Dr Benjamin C Rosenthal, 140
New York Ave, Brooklyn 16
Place Kings County Medical Society Bldg, 1313 Bedford
Ave Time Third Thursday in February, April,
May, October and December

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President Dr Walter F King, 519 Delaware Ave,
Buffalo
Secretary-Treasurer Dr Sheldon B Freeman, 196
Linwood Ave, Buffalo
Time Second Thursday of each month

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OTOLARYNGOLOGY**

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Secretary Dr Douglas Chamberlain, Chattanooga
Bank Bldg, Chattanooga, Tenn
Place Mountain City Club Time Second Thursday
of each month from September to May

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President Dr Vernon M Leech, 55 E Washington
St, Chicago
Secretary Dr W A Mann, 30 N Michigan Ave,
Chicago
Place Chicago Towers Club, 505 N Michigan Ave.
Time Third Monday of each month from October
to May

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STAFF**

Chairman Dr D T Vail, 441 Vine St, Cincinnati
Secretary Dr A A Levin, 441 Vine St, Cincinnati
Place Cincinnati General Hospital Time 7 45 p m,
third Friday of each month except June, July and
August

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Chairman Dr Shandor Monson, 1621 Euclid Ave,
Cleveland
Secretary Dr Carl Ellenberger, 14805 Detroit Ave,
Cleveland
Time Second Tuesday in October, December, February
and April

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Clerk Dr George F J Kelly, 37 S 20th St,
Philadelphia
Time Third Thursday of every month from October
to April, inclusive

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Chairman Dr H D Emswiler, 370 E Town St,
Columbus, Ohio
Secretary-Treasurer Dr D G Sanor, 206 E State
St, Columbus, Ohio
Place The Neil House Time 6 p m, first Monday
of each month

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Bldg, Corpus Christi, Texas
Secretary Dr L W O Janssen, 710 Medical Professional
Bldg, Corpus Christi, Texas
Time 6 30 p m, third Tuesday of each month from
October to May

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OTO-LARYNGOLOGY**

President Dr Ruby K Daniel, Medical Arts Bldg,
Dallas 1, Texas
Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,
Texas
Place Dallas Athletic Club Time 6 30 p m, first
Tuesday of each month from October to June The
November, January and March meetings are devoted
to clinical work

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 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa
 Time 7 45 p m, third Monday of every month from September to May

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Chairman Members rotate alphabetically
 Secretary Dr Cecil W Lepard, 1025 David Whitney Bldg, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time First Wednesday of each month, November to April inclusive

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President Dr Raymond S Gouw, 545 David Whitney Bldg, Detroit 26
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit 26
 Place Club rooms of Wayne County Medical Society
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

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 Time Third Wednesday in October, November, March, April, May and June

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 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

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AND OTO-LARYNGOLOGICAL SECTION**

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

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LARYNGOLOGICAL SOCIETY**

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 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

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OTO-LARYNGOLOGY**

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

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THROAT SOCIETY**

Chairman Dr Harold Snow, 614 S Pacific Ave, San Pedro, Calif
 Secretary-Treasurer Dr Oliver R Nees, 508 Times Bldg, Long Beach, Calif
 Place Professional Bldg Time Last Wednesday of each month from October to May

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OTOLARYNGOLOGY**

President Dr M E Trainor, 523 W 6th St, Los Angeles
 Secretary-Treasurer Dr Orrie E Christ, 210 N Central Ave, Glendale, Calif
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

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THROAT SOCIETY**

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 Secretary Dr James J Monahan, 31 S Jardin St, Shenandoah, Pa

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 Secretary Dr Frazier Williams, 1801 I St N W, Washington
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

**MEMPHIS SOCIETY OF OPHTHALMOLOGY AND
OTOLARYNGOLOGY**

Chairman Each member in alphabetical order
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Leon H Guerin, 324 E Wisconsin Ave, Milwaukee 2
 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2
 Place University Club Time 6 30 p m, fourth Tuesday of each month from October to May

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 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

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President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada
 Time Second Thursday of October, December, February and April

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 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

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 Secretary Dr Frederick A Wiess 255 Bradley St, New Haven, Conn

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 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

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 Secretary Dr Wendell L Hughes, 131 Fulton Ave, Hempstead, N Y
 Time 8 30 p m, third Monday of every month from October to May, inclusive

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 Secretary Dr Benjamin Esterman, 983 Park Ave, New York
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday of each month from October to May, inclusive

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 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City
 Place University Hospital Time Second Tuesday of each month from September to May

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President Dr D D Stonecypher, Nebraska City, Neb
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia
 Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia
 Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr George H Shuman, 351-5th Ave, Pittsburgh
 Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Michael J Penta, 312 N 5th St, Reading, Pa
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

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President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va
 Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis
 Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis
 Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except December

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President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas
 Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine, Randolph Field, Texas
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center
 Time 7 p m, second Tuesday of each month from October to May

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SECTION ON EYE, EAR, NOSE AND THROAT**

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco
 Secretary Dr A G Rawlins, 384 Post St, San Francisco
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

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President Dr David C Swearingen, Slattery Bldg, Shreveport, La
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September

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 Secretary Dr Clarence A Veasey Jr, 421 W Riverside Ave, Spokane, Wash
 Place Spokane Medical Library Time 8 p m, fourth Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St, Syracuse, N Y
 Secretary-Treasurer Dr I H Blasdell, 713 E Genesee St, Syracuse, N Y
 Place University Club Time First Tuesday of each month except June, July and August

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr E W Campbell, 316 Michigan St, Toledo, Ohio
 Secretary Dr L C Ravin, 316 Michigan St, Toledo, Ohio
 Place Toledo Club Time Each month except June, July and August

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr W R F Luke, 316 Medical Arts Bldg, Toronto, Canada
 Secretary Dr W T Gratton, 216 Medical Arts Bldg, Toronto, Canada
 Place Academy of Medicine, 13 Queens Park Time First Monday of each month, November to April

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President Dr S Bockoven, 1752 Massachusetts Ave, Washington, D C
 Secretary-Treasurer Dr John Lloyd, 1218-16th St N W, Washington, D C
 Place Medical Society of District of Columbia Bldg, 1718 M St N W, Washington, D C Time 7 30 p m, first Monday in November, January, March and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn
 Secretary Dr Samuel T Buckman, 70 S Franklin St, Wilkes-Barre, Pa
 Place Office of chairman Time Last Tuesday of each month from October to May

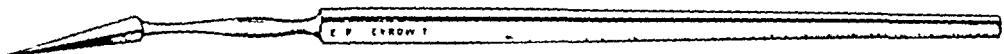
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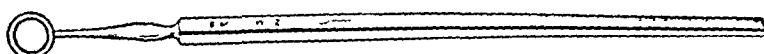
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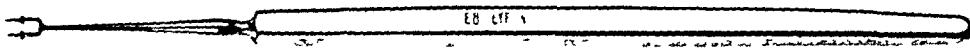
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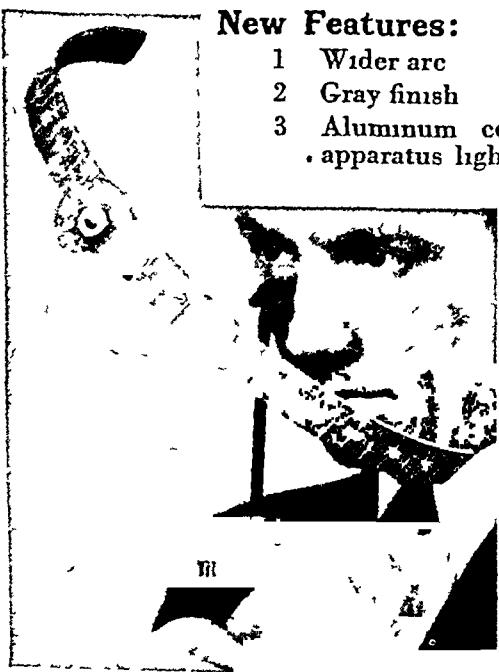
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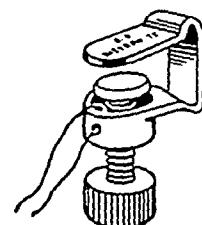
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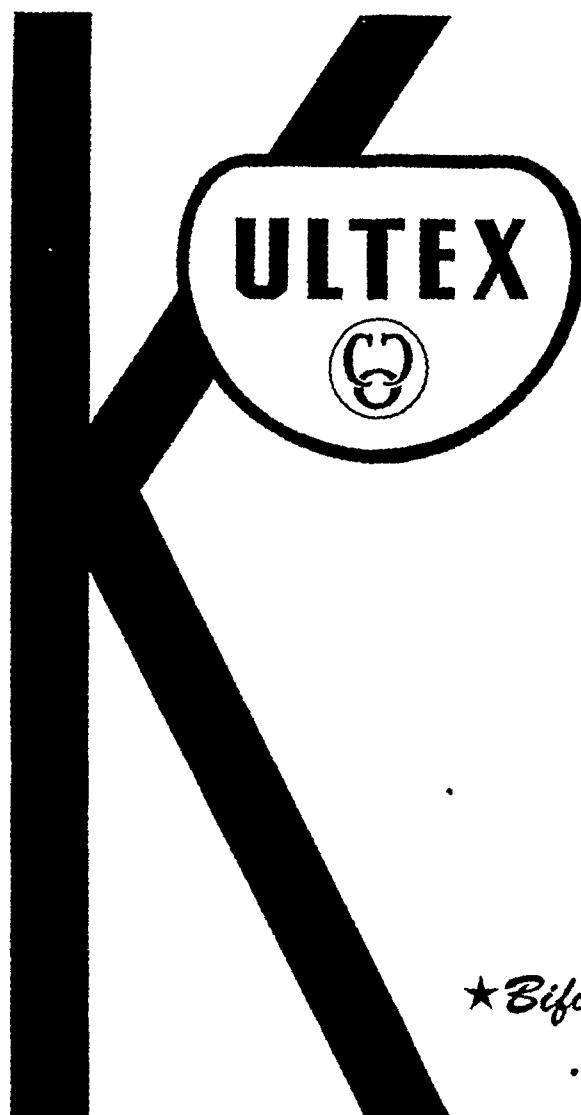
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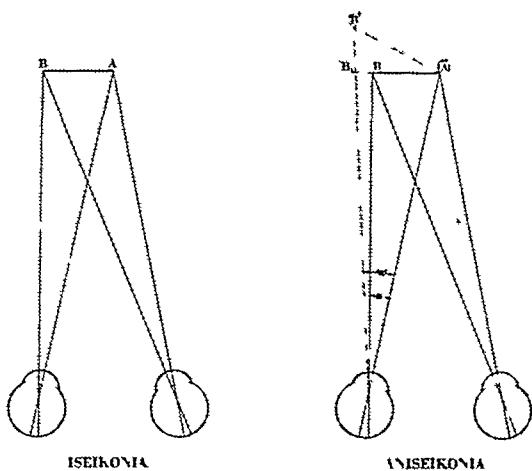
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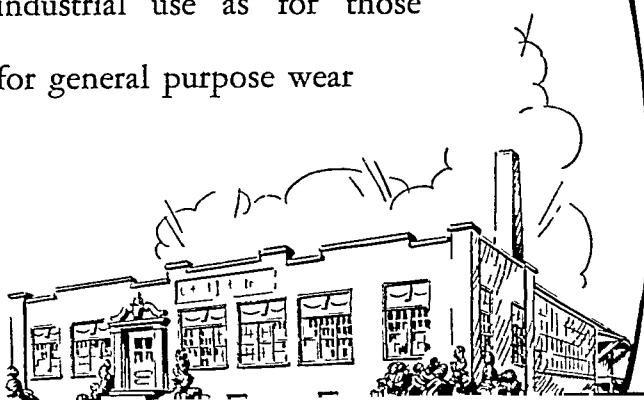
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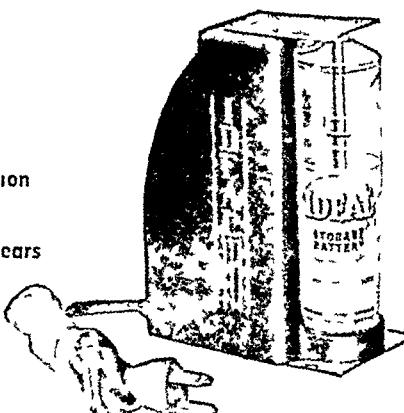
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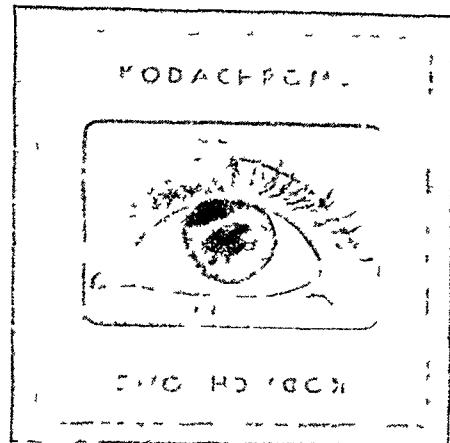
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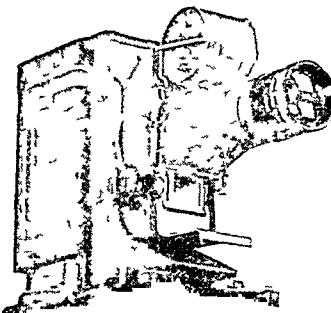
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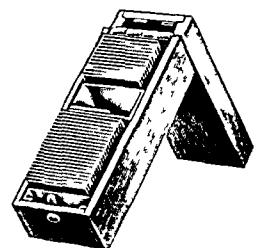


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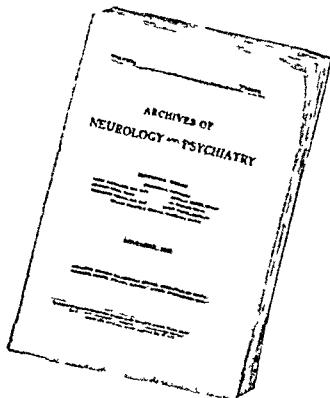
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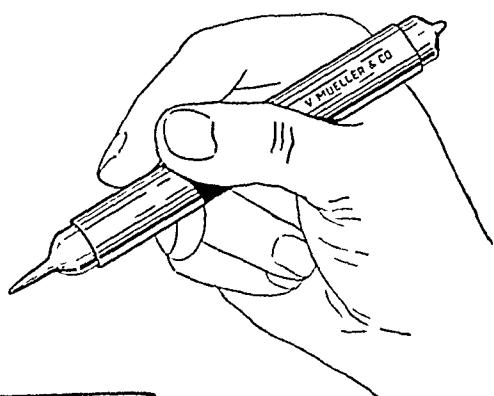
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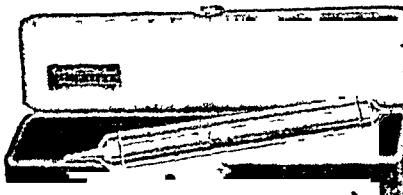
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